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Faculty of Medicine and Health Sciences
Universiti Malaysia Sabah
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Tel: +60 88 320000 Ext 5620
Fax: +60 88 320928
Email: bjms@ums.edu.my

PUBLISHER

Penerbit Universiti Malaysia Sabah (UMS)
Ground Floor, Library
Universiti Malaysia Sabah
Jalan UMS
88400 Kota Kinabalu
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Tel: +60 88 320 789
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EDITORIAL

Dengue!!! A Current Threat with Previous Experience

Sadia Choudhury Shimmi[1], Mohd Yusuf Ibrahim[2, 3], Kamruddin Ahmed[2, 4]

[1] Department of Biomedical Science and Therapeutics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[2] Borneo Medical and Health Research Centre
[3] Department of Community and Family Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[4] Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

Keywords:
dengue, threat, current

Dengue is a global health problem. Some countries describe it as 'endemic' where other countries as 'epidemic' according to the prevalence of the disease[1]. Dengue virus transmitted by the infected female *Aedes aegypti* and *Aedes albopictus* mosquitoes, belongs to the genus Flavivirus which is an envelope positive-sense single-stranded RNA virus. Rainy season (June to October) is the prime time of spreading the infection in Southeast Asia. Four serotypes of dengue viruses (DEN-1, DEN-2, DEN-3 and DEN-4) are able to infect humans and cause dengue haemorrhagic fever/dengue shock syndrome like severe infections. Moreover, cross-reactive antibodies (IgM and IgG) produce against other serotype when infection occurs with one serotype. This is one of the diagnostic problem for acute dengue[2]. Some researchers experienced that without warning signs and mild symptoms were found in DEN-1, severe dengue was found in DEN-2 patients as compared to other serotypes and musculoskeletal symptoms were prominent in DEN-3 infected patients. So that different receptors or organs are targeted to establish infection by different dengue serotypes[3]. This virus circulates in the blood of an infected person for 2 – 7 days, at that time the infected person develops a fever. After appearance of the first symptoms (for 4 – 5 days; maximum 12 days), infected patients can transmit the infection via Aedes mosquitoes[1]. Clinical presentation of dengue virus infection in humans ranging from clinically asymptomatic or transient

nonspecific febrile illness to classical dengue fever (DF) and dengue haemorrhagic fever/ dengue shock syndrome (DHF/ DSS). Fever, headache, rash, bone and muscle pains with or without abdominal pain are the general clinical presentation of patients with DF and early DHF/DSS. Haemorrhagic manifestations such as haematuria, bleeding gums, epistaxis, hematemesis, melena, and ecchymosis develop in DHF. DHF patients develop thrombocytopaenia and haemoconcentration. Some patients may progress into DSS, leading to profound shock and death if not diagnosed or treated properly[2].

Among the major health problems in the Southeast Asia, dengue was one of them since 1950's. Malaysia experienced first dengue case in 1902[4]. Major outbreaks in Malaysia were in 1974, 1978, 1982 and 1990. In Malaysia, maximum number of dengue cases were observed between 2014 and 2017. A total of 108,698 dengue cases were reported in Malaysia in 2014. This number was decreased to around 101,357 in 2016 but the mortality rate was 10% higher than that of 2014. The dengue situation in Malaysia came under in 2017. However, the number was still greater than that in 2013[5, 6].

According to WHO (2019), the cumulative number of cases of dengue reported as of 10 August 2019 was 82,529 including 120 deaths in Malaysia. This is higher compared to 44,613 cases with 73 deaths reported during the same period last year[1]. It was found that 251 hotspots for dengue mainly in nine states Selangor, Sabah, Penang, Sarawak, Federal Territories, Kelantan, Johor, Pahang and Negeri Sembilan where most of the hotspots were flats and apartments[7]. Among the states, Sabah recorded 2,707 dengue cases with six deaths up to July 2019, Sandakan was the highest and Tawau stood second in number of cases with five deaths[8]. Some researchers observed that circulating serotypes was changing within different years. In 2014, DEN-1 was predominant in Sabah whereas in 2015, DEN-2 was predominant[9]. In Sandakan, DEN-1 was the predominant serotype in 2018 according to some investigators. Again, they found co-infection with more than one DEN serotypes[10].

Not only Malaysia, Vietnam also reported more than 105,000 dengue fever patients with 10 death. Thailand reported 49,174 cases with 64 deaths. In Bangladesh, Myanmar, Cambodia, and Laos fatal dengue cases are also increasing this year. Bangladesh is experiencing its biggest outbreak in two decades with at least 40 people dead. According to Bangladesh's Ministry of Health, a total of 43,271 dengue patients in Bangladesh from January to August of this year. As in Myanmar, more than 3,100 cases and at least 10 deaths were recorded, while 13,000 cases of dengue fever from January to June were recorded by Cambodia. In Laos, 11,561 people were diagnosed with dengue fever and 27 died[11].

Recently, Malaysian Government has implemented a National Dengue Plan (2015 – 2020) for early detection and measure for the infection during the course of an outbreak. According to many studies in this field, viral factors is one of the risk factors and components of interest. Shifting of dengue serotypes and genotypes may contribute to the increasing number of dengue cases due to an antibody-dependent enhancement (ADE) effect. Several measures have been taken by Government for the prevention of dengue such as fogging and removing mosquito breeding sites[3].

Prevention is better than cure. Preventive measure should be taken as well as early detection of circulating serotypes that could help to prevent serious dengue clinical outcomes during outbreaks.

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REVIEW ARTICLE

Apoptosis: Dual Role in Aetiology and Cure

Aye Aye Wynn*[1], Ohnmar Myint[1], Nang Khin Mya[1]

[1] Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: drwynnaa@ums.edu.my

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ABSTRACT

Apoptosis is a programmed cell death which occurs following a variety of stimuli. Physiologically the process is important for morphogenesis of organs and homeostasis of different types of cells. Apoptotic cell death is responsible for a variety of pathologic states such as elimination of cell death in mutated cells, infected cells, tumour cells and transplant rejection well as the pathological atrophy. In this review, there is discussion about the control of apoptosis, detection methods of apoptosis, its association with infectious and non-communicable diseases. Intracellular microorganisms survive through inhibition of host cell apoptosis as well as they destroy the parenchymal cells causing impaired functions. It plays important role in tumourigenesis. There are possible therapeutic roles of drugs that modify apoptosis in human diseases.

INTRODUCTION

Apoptosis is a process of programmed cell death and the word was derived from Greek word meaning "falling off" which is an analogy to leaves falling off trees[1]. Apoptosis follows a specific stimulus and stimulated by rapid activation of endonucleases[2 – 4]. It is a physiological process occurring during organogenesis in embryonic life, tissue homeostasis such as atrophy of cells in senility, shrinkage of breast and reproductive organs after reproductive period. It has a role in some pathological conditions such as removal of DNA damaged cells and immune cells on removal of cytokines and growth factors[5, 6].

Recent studies found that some DNA lesions such as base-alkylations, DNA cross-links and DNA-double-strand breaks (DSBS) can trigger apoptosis[7]. Programmed cell death is initiated by activations of endonucleases which causes proteolysis of DNA repair proteins, cytoskeletal proteins, and the inhibitor of caspase-activated deoxyribonuclease[8, 9].

Detection of Apoptosis

Histologically apoptotic cells are characterized under light microscope by cell shrinkage, blebbing of plasma membrane, small fragmentation of cell cytoplasm containing pyknotic remnants of nuclei. It can also be detected by terminal deoxynucleotidyltransferase (TdT) mediated dUTP-biotin nick end labelling (TUNEL) method to see the nuclear fragmentation[10] which is based on specific binding of TdT to 3'-OH ends of DNA of nuclei undergoing apoptosis on the histological sections or cell preparation in flow or laser scanning cytometry[10, 11]. Degradation of genomic DNA results in formation of DNA fragments which on agar rose electrophoresis show laddered DNA[12]. Ligation-mediated polymerase chain reaction (LMPCR) can amplify DNA fragmentation specific to apoptotic cell death[13, 14]. Ultrastructurally, nuclear chromatin condensation, cells break up into membrane-bound bodies, apoptototic bodies, which are phagocytosed and degraded by cells such as histiocytes, endothelial cells, epithelial cells or neoplastic epithelial cells[1, 13]. Oligonucleotide and protein microarray methods detect the genes and proteins that regulate apoptosis through the Fas system[15, 16].

Control of Apoptosis

Apoptosis is initiated by the extrinsic pathway, which can be triggered by ligation of death receptors which activates caspase-8 and the intrinsic pathway initiated by cellular stress by activation of caspase-9 following the cellular stress or the granzyme B pathway, which uses granzyme B to kill the target cells[17]. Double-strand specific caspase is activated and cleaves the chromosomal DNA into large fragments of 50 – 300 kb[18]. Some studies describe about the caspase independent processes which requires apoptosis inducing factor (AIF)[17]. There are many genes identified in recent years which are responsible for apoptosis[20]. *Bcl2* oncogene promotes cell survival by blocking programmed cell death that prevents the permeability of mitochondrial outer membrane[21]. Mutation of transmembrane receptor protein, CD95/Fas, that interact with Fas associated death domain (FADD) to recruit pro-caspase 8[22]. Bax which is a bcl2 homologous protein when stimulated inserts into the mitochondrial outer membrane to release cytochrome C in apoptosis. P53 has a major role in inducing apoptosis: it regulates cell cycles by allowing damaged DNA to repair, inducing Bax expression[23], through activation of Noxa[24], increasing the level of reactive oxygen radicals (ROS), all of which can trigger release of cytochrome C. Inhibitors of apoptosis proteins (IAPs) are composed of 70 amino acids termed BIR (baculoviral IAP repeat) discovered in genome of baculoviruses[25]. Cyclin D1 promotes cell proliferation and inhibits drug-induced apoptosis[26]. Apoptotic peptidase activating factor-1 (Apaf-1) is responsible for initiating apoptosis downstream mitochondrial damages. Loss of expression of Apaf-1 is associated with recurrences of cancer[27].

Apoptosis and Non-communicable Diseases

Apoptosis is a very important process in development of mammals. It deletes some organs during organogenesis, controls the number of cells, elimination of potentially dangerous cells. Mutation of FANCC, which has effects on the failure of apoptosis of haemopoietic stem cells (HSC) on exposure to growth factor deprivation causing DNA damage, is described in Fanconi anaemia (FA)[28]. Defective Fas-induced apoptosis can lead to autoimmune lymphoproliferative syndrome in human[29] which present with

reactive lymphadenopathies and autoimmune manifestations. Apoptosis plays a role in pathogenesis of gout. Delayed spontaneous and TNF-a induced apoptosis is observed in acute gouty arthritis[30] and renal damage is caused by apoptosis of renal tubules induced by uric acid[31]. Mutation of p53, a gene that blocks the damaged cell to enter cell cycle and directs towards apoptosis, leads to genetic instability characteristic of many cancer cells[2]. Apoptosis and the genes that control it have a significant effect on the carcinogenesis in the steps of initiation and progression, tumour biological behaviour such as metastasis and the morphologic types of cancer[22]. Mutation of caspase-8 gene is associated with advanced gastric cancer, hepatocellular carcinoma[32] leukaemia[33] and medulloblastoma[34]. Bcl-2, a protein that blocks apoptosis, is associated with B cell lymphoma and inhibitors of apoptosis proteins (IAPs) is found in MALT lymphoma[35]. Massive and selective apoptosis lead to neurodegenerative diseases and neural tube defects[36]. Mutation of neuronal apoptosis inhibitory protein (NAIP) was shown in spinal muscular atrophy[37]. Apoptosis of cardiomyocytes induced by non-encoding RNAMeg3 is associated with myocardial infarction and biomarkers of cell death such as MAC were studied in post-mortem cases in an attempt to identify the new diagnostic markers[38, 39].

Apoptosis and Infections

Bacteria-induced host cell death by apoptosis to enhance their replication and survival[40]. Intracellular organisms such as *L. pnemophilia*, and *Chlamydia* spp. survive in their host cells by inhibiting the macrophage apoptosis[41]. A mutant gene nuoG in *M. tuberculosis* decreased the ability to inhibit macrophage apoptosis and subsequently reduced the virulence of the organism[42]. Bacterial infection of central nervous system with group B Streptococcus lead to apoptosis of neurons in the presence of microgli[43]. Regeneration of neural tissue occurs after injury, but it is not sufficient to replenish the cells required for normal function. Apoptosis and necroptosis of neurons and glial cells occur in meningitis and it is responsible for neurological complications[43]. HIV 1 virus evades macrophage apoptosis by transcription of prosurvival genes via MAP2K1/ERK2 pathway[44]. Placental malaria usually complicated by poor neonatal outcome due to growth retardation is related to apoptosis-related mechanism[45]. Hepatitis B and C viruses cause chronic liver disease and parenchymal damage by escaping viral clearance by apoptosis[46]. Levels of Caspase-3, which triggers apoptosis, are low in *Mycobacterium tuberculosis* infected pulmonary alveolar macrophages rendering them to escape from apoptosis and create a more favourable environment for intracellular growth of bacteria[47]. Apoptosis is both qualitatively and quantitatively increased in lepra type 1 reaction and proposed to be one of the variables for high detection of the reaction[59] and lepromatous leprosy[48]. High level of nerve growth factor (NGF), a neurotrophin that causes apoptosis of Schwann cells and nerve damage, is correlated with nerve damage[49]. Pathogens like *Leptospira interrogans* escape phagocytosis by rendering apoptosis of macrophages through Fas-FasL/Caspase-8/-3 pathway[49].

Application in Therapeutics

Apoptosis is involved in tumourigenesis and other human diseases, it is also a centre of target for treatment. Inhibitors of apoptosis such as IAP may serve as a molecular target for specific anticancer therapy. IAPs can also be used as an indicator of prognosis after therapy as highly expressed in tumour cells[50]. IAP counter-reacts the high basal caspase activity of tumour cells selectively[51, 52]. Survivin, a member of IAP, is implicated management of cancer in different aspects such as targeting the tumorgenesis, neovascular angiogenesis, and immunotherapy target. Recombinant survivin protein used as a immunotherapy was effective as an adjuvant therapy in human melanoma cells[53, 54]. Some advances have been made to focus on TNF-related

apoptosis-inducing ligand (TRAIL) for cancer treatment[55]. Agonistic antibodies to TRAIL receptors can induce apoptosis of the tumour cells. Antiapoptotic- Bcl-2 family proteins are implicated in indicators of chemotherapy resistance in prostate cancer and other solid cancers and haematological malignancies[56]. Parenchymal cell death in diseases is a major concern in treating many diseases. Caspase-8, after activation by caspase cascade, is responsible for tumour cell motility by acting on focal adhesion complexes[57]. Evidence showed that pan-caspase inhibitors have profound effect on acute TNF- and Fas/FasL mediated apoptosis in hepatocytes and caspase mediated metastasis[57]. Short term uses of inhibitors of apoptosis are implicated in conditions such as ischaemic stroke, spinal cord injury, reperfusion injury and organ transplant. Arthritis, Alzheimer's disease, and Huntington's disease may benefit from their long-term usage[58]. Anti-angiogenic cancer therapy targets the vascular endothelial cells by inducing the Fas-ligand and initiating the apoptosis cascade[59]. Understanding the underlying mechanisms such as MAP2K1/ERK2 pathway and host cell K+ channels inhibition helps to design effective antiviral drugs for HIV and HCV[44, 46].

CONCLUSION

Apoptosis, programmed cell death, is an essential process in development, control of immune system and tissue homeostasis in living. In addition to its physiological functions, it also plays a role in aetiology of tumour formation and in the mechanism to reduce tumour cell burden in cancer caused by apoptosis of tumour cells. However, there are still some controversial theories on the use of apoptosis modifying therapeutics. Attempts should be made to consider several therapeutic aspects of apoptosis to improve the patient's outcome.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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ORIGINAL ARTICLE

Alcohol Toolkit: Empowering Sabah Indigenous Communities to Reduce Alcohol-Related Harm

Helen Benedict Lasimbang[1*], Liz Eckermann[2], Wendy Shoesmith[1], Sandi James[3], Aisat Ellik bin Igau @ Oswald Iggau[4], Lee Kuok Tiung[5], Jephte Sompud[6], Asong Joseph[1]

[1] Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[2] School of Humanities and Social Sciences, Deakin University of Australia
[3] Faculty of Health, Science and Engineering, La Trobe University, Victoria, Australia
[4] Faculty of Business, Economics and Accountancy, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[5] Faculty of Humanities, Arts and Heritage, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[6] Faculty of Science and Natural Resources, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: hbl66@ums.edu.my

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ABSTRACT

Alcohol misuse compromises the quality of life of individuals, families, communities and whole societies in a variety of ways. Malaysia acknowledges the problems, implementing policies and health promotion activities in line with the World Health Organization Global Strategy to reduce the harmful use of alcohol by 10% between 2010 and 2025. Sabah, one of two Malaysian states on the island of Borneo, has more than 30 different indigenous ethnic groups. Alcohol production and consumption have traditional and unique roles in the cultural practices of many of these groups, making one common programme difficult to implement. Preliminary research suggests that alcohol is a serious problem in indigenous communities in Sabah. It also shows lack of knowledge on recommended limits for alcohol consumption and understanding of alcohol-related harm. The objective of this action-research is to produce a toolkit that will transfer knowledge and empower communities to adopt safer drinking and reduce alcohol-related harm. It must be attractive, appropriate, easily understood and be able to be tailored to suit different communities. The alcohol tool-kit was developed by a group of academicians using evidence-based information. Qualitative research methods were used to evaluate the initial alcohol tool-kit. A purposive sample of 45 village representatives was selected and divided into 5 groups for focus group discussion. Their feedback was recorded and transcribed verbatim. The alcohol tool-kit was edited accordingly. All participants agreed the alcohol tool-kit was important and can empower communities to reduce alcohol-related harm directly improving their quality of life. The amended alcohol tool-kit will be recommended for health promotion material and evaluated from time to time.

INTRODUCTION

The harmful use of alcohol causes significant burden to individuals, families and societies[1]. According to the WHO fact sheet on alcohol, in 2015 the harmful use of alcohol directly or indirectly caused 3.3 million deaths. This represents around 5.9% of all deaths worldwide every year. It is also reported to be the cause of more than 200 diseases and injury conditions[2]. Apart from the health consequences, excessive use of alcohol has been shown to result in social and economic consequences[3]. The consequences of alcohol consumption depend on the volume consumed, pattern of drinking and the quality or type of alcohol being consumed[4]. There are wide and varied reasons for why people consume alcohol. It has been used for centuries in these cultures for spiritual purposes and celebrations, as well as for relaxation and socialization[5].

The population of Malaysia is about 30 million, of which 61.3% are Muslim[6]. Alcohol consumption is prohibited in Islam[7] which may explain the low prevalence of 7.7% of alcohol consumption reported in this country[8]. The highest prevalence occurs in Kuala Lumpur, followed by Sarawak and Sabah[8, 9]. Sarawak and Sabah are Malaysian states located in East Malaysia, on the island of Borneo. They differ from the states located in West Malaysia because the population is mostly comprised of large indigenous communities where alcohol plays an important role in their cultural traditions[10]. Although the overall prevalence of alcohol consumption in Sabah and Sarawak is low[11], it has been reported that 50% of those who consume alcohol drink in ways considered to be harmful[11]. Mutalip et al. (2014)[11] also reported that among those who drink, 23.6% drink in risky ways. High-risk drinking was noted to be more prevalent among rural drinkers, indigenous peoples of Sabah and Sarawak, low education and low income households[11]. In Sabah, locally brewed (unrecorded) alcohol such as *montoku*, *tapai*, and smuggled alcohol are cheaply available [12]. Research on alcohol in this region is scarce, preventing an accurate picture of the magnitude of alcohol-related harm in Sabah. However, it is common to read reports in newspapers about alcohol-related harm such as domestic violence, motor-vehicle accidents, and fights[10]. It is noted that alcohol plays a significant role in many presentations to the psychiatric hospital in Sabah. Alcohol is also a contributing factor in relapse of mental illness in some individuals. The government of Malaysia acknowledges the problems related to alcohol use and has introduced various strategies to address this issue[13]. In 1976 the Malaysian Government introduced drink driving laws and penalties. In 1979 the excise act was implemented, and in 2010 they included abstaining from alcohol as part of a healthy lifestyle campaign[14]. A national action plan (2013 – 2020) was also created with the intention to prevent and reduce alcohol-related harm[15].

The serious burden of alcohol to individuals and communities in most countries has made it an international issue. In 2010, during the 63rd World Health Assembly, the harmful use of alcohol worldwide was one of the four public health issues discussed. This assembly also endorsed the global strategy to reduce the harmful use of alcohol[4]. The strategy includes extensive and detailed evidence-based guides for global, regional, national and community-based interventions[4]. The outcomes of the various strategies to reduce alcohol related harms are unique depending on the local context[16, 17, 18]. It is suggested that community-based and bottom-up prevention measures are the most effective strategies to reduce drinking and alcohol related problems[19, 20, 21, 22].

In Sabah, the large number of different ethnic groups makes one single programme difficult to implement. Strategies that are appropriate and work in one population may not be appropriate for another population. There is a need for a tailored strategy that is appropriate and acceptable for multi-ethnic

communities; one that is accepting of local cultural traditions; and meets communities and individuals where they currently are in terms of understanding and desire for change. The limitations of abstinence-based approaches where individuals and communities are not interested in abstinence can be addressed where communities are interested in reducing the problems caused by alcohol[23, 24]. Alcohol harm reduction has been shown to be an effective approach when it is part of a comprehensive policy package, addressing all levels of policy and practice and considering the communities needs and wishes[25]. Top down approaches, where the communities are not involved and government policies are made without consideration of the local context, appear to have little effect in rural and remote communities[26].

The overall objective of this project was to produce a community-inclusive tool-kit that will transfer knowledge and empower communities to adopt safer drinking and reduce alcohol-related harm.

MATERIALS AND METHODS

This action-research was divided into two phases from February 2016 to August 2017. The first phase of the project was the development of the 'alcohol intervention tool-kit' using available evidence-based data[4, 26, 27]. A tool-kit tailored for the indigenous communities of Sabah was developed by a team comprising of local NGOs and academicians in early 2009[10]. This initial 'alcohol intervention tool-kit' was given to several indigenous communities and they reported it was somewhat useful in reducing alcohol-related harm. However, this initial 'tool-kit' was not formally reviewed nor adapted to suit the individual communities. It was considered alongside other data, programmes and activities already existing in Sabah. This information was then collated into booklets, each booklet addressing a different topic related to alcohol harm reduction. Collectively it was called 'alcohol tool-kit' (Figure 1). The final alcohol tool-kit was one introductory pamphlet and a set of 7 booklets (Table 1). Bahasa Malaysia was used for the booklets because more than 90% of the target population can read and speak this language[28].

Figure 1 Alcohol toolkit

Table 1 Content of the alcohol tool-kit

Number	Content
1	Introduction to alcohol tool-kit
2	Topic 1: Making choices to drink or not to drink?
3	Topic 2: You and alcohol
4	Topic 3: General knowledge about alcohol
5	Topic 4: Alcohol and culture
6	Topic 5: Reducing alcohol-related harm
7	Topic 6: A guide to changing your drinking habits
8	Topic 7: My achievement diary

The second phase was the evaluation of the 'Alcohol Tool-kit'. A qualitative research method was used, and the data was collected with thematic interview to evaluate the attractiveness, appropriateness, and understanding of the alcohol tool-kit. These indicators were selected through discussion to ensure the tool-kit had the best possible chance of uptake in the target communities. Purposive sampling was used to achieve maximal variation, with participants selected from various backgrounds in terms of age, occupation, gender and position in the village. A one-day workshop was organized for phase 2 to ensure that ample time was given to discuss in detail the various aspects of the tool-kit. At the beginning of the workshop, all participants were given an introductory talk on the toolkit and the objectives of the workshop.

The participants were encouraged to join the group they were comfortable with. There were 5 groups with 9 participants in each group. This was to ensure the opportunity for varied inputs from all participants. The facilitators were academicians and trained members of the community. The summary of participants' socio-demographic profiles is shown in Table 2.

Table 2 Socio-demographic of participants who participated in the Alcohol Tool-kit evaluation

Demography	*N* = 44	%
Gender		
Male	19	43.2
Female	25	56.8
Age		
19 – 30	5	11.4
31 – 40	8	18.2
41 – 50	17	38.6
51 – 60	14	31.8
Religion		
Christian	42	95.5
Muslim	2	4.5
Ethnic		
Kadazandusun	44	100
Occupation		
Farmer	15	34.1
Housewife	3	6.8
JKKK	7	15.9
Teacher	1	2.3
Clerk	1	2.3
Retired	1	2.3
Not stated	16	36.4

The briefing and interview guide was given to the facilitators to ensure uniformity of the discussion. Participants discussed, commented and gave suggestions based on attractiveness, appropriateness, the ease of readability and understanding, so the booklets would be more effective for the community. Notes and a summary of their answers were recorded and presented to all participants by one selected member from each group. This enabled the other groups to give further input or debate issues of conflict. The community input was documented and summarized. Inductive content analysis was completed using Atlas.ti7. The feedback and input were incorporated in the final version of the alcohol toolkit. Ethical permission was taken [JKEtika1/16(2)].

RESULTS

All participants acknowledged that alcohol-related harm is a problem in their village. During the workshop, participants agreed that

the information in the toolkit was relevant and important. They agreed that it would be helpful in encouraging and supporting the communities to reduce alcohol-related harm. The community input was summarized into four main themes.

Attractiveness

Participants from all five groups commented that the covers of the toolkits were dull and boring. They suggested adding pictures, colours and improving the paper quality of the cover. All participants proposed to include more pictures and increase the font size. They also suggested that using real pictures of local communities would make the toolkit more attractive and relevant.

Appropriateness

All groups commented that illustrations depicting foreigners in the tool-kit was inappropriate. They suggested to pictures of local people would be more appropriate. Two of the groups expressed that they did not appreciate seeing a picture of a drunken dog in the booklet and wanted it to be removed. They stated that they considered it humiliating and not an appropriate way to illustrate the point at hand. One group suggested that the standard alcohol unit be stated in Kadazandusun as well as Malay. Another group suggested that the toolkit on 'Making a choice: Should I drink alcohol or not?' should be the first booklet in the toolkit rather than the fourth. This booklet is aimed towards adolescents that have not yet started drinking. The goal is to help empower them to make healthy choices regarding the use of alcohol. Two of the groups felt that cartoons depicted playfulness and were not appropriate for certain sections due to the seriousness of the topic. They stated they would prefer the illustration dialogue to be constructive and serious and avoid sarcasm or humour.

Ease of Readability and Understanding

All the participants agreed that the content of the toolkit is simple, clear and informative. The language is easy to understand and accessible and useful for people of all ages. They found some words difficult to understand; such as "*piawai*" (standard), "*akut*" (acute) and "*toolkit*". Two out of five groups stated that it is not necessary to repeat 'one standard alcohol drink' in all booklets in the toolkit. These concerns were discussed. This concept is new to these communities and is considered important for reducing alcohol-related harm. The working group agreed that 'one standard alcohol drink' is an integral component of the educational side of the booklets and that it is an important concept that needs to be repeated. To place this into a local context was also noted an important path to it being taken up by the communities.

Additional Comments to Make the Toolkit More Effective

The leaders (or heads) of the villages suggested to include information about native customary law. A section in Kadazandusun native law provides information for community and community leader responses and consequences for negative behaviour due to alcohol intoxication. It was also suggested to add a table of contents and acknowledgements.

DISCUSSION

The communities welcomed the team openly and with enthusiasm. Possible reasons this occurred so readily include: the team had involved the communities in the discussions and development of the tool-kit; the team did not enter the community to impart knowledge onto the people, but rather as seekers of knowledge and collaborators in the process; *the team asked the community for their assistance to develop a toolkit that would address their needs, rather than stating a problem and giving directions on what

needed to be changed; participants were respected as holders of the knowledge on what was needed and which intervention strategies might work within their community. They had acknowledged that alcohol was causing problems in their society and were seeking ways to solve it.

Participants were drawn from various backgrounds, educational levels, and occupations, as well as positions within the community. No difficulties were reported from any of the participants related to understanding the information in the toolkit. Literacy problems were overcome by reading the material in a group. Discussion of the tool-kit contents along with the illustrations and tables enabled sufficient access to the material by all participants. The participants were very cooperative, actively involved and remained for the duration of the workshop. The importance of community participation and input was demonstrated in this workshop. This was to ensure the communities were an active part of the tool-kit development and claimed some ownership over its development[28].

Participants spoke about how some of the information and illustrations in the toolkit were not acceptable for their community, despite being thought to be appropriate by the academic team. For example, people felt that the cartoons portrayed playfulness and minimized the seriousness of the subject. They felt it was more suitable for the booklet aimed at young people. Participants stated that the use of images of foreigners in the illustrations seemed inconsistent with the aim of the Tool-Kit. The academic team had considered this point prior to the workshop but decided to include those images due to lack of access to alternative images.

During the workshop, participants were involved to address alcohol issues in the communities. This enabled them to feel heard, respected and motivated to participate actively in reducing alcohol-related harm. Participants also learned and gained knowledge about alcohol while reviewing the alcohol toolkit. This increase of knowledge also allows "word of mouth" communication of the importance of alcohol harm reduction, enables communities to identify problems and difficulties and feel confident in beginning to tackle these issues.

The academic team was not previously aware of the importance of including native customary law in the toolkit. People knowledgeable in this area were subsequently consulted and customary law then included in the alcohol tool-kit booklets. Tailoring a programme or intervention to be culturally appropriate and relevant for the populations can make it more effective[29, 30]. The WHO global strategy to reduce alcohol-related harm has recommended community involvement and engagement as an important strategy. This project initially started with academics developing the toolkit without the communities' feedback or input. Involving the community in the further development of the toolkit increased the acceptance of this intervention. It gave the communities a sense of ownership and increased its implementation and availability.

Challenges in Tailoring the 'Alcohol Tool-kit'

As noted above, some participants were illiterate which made accessing the materials difficult. The team needs to further consider appropriate methods that could overcome this barrier once the toolkit is distributed into the communities. To be an effective strategy in the communities, the toolkit needs to be printed in sufficient quantity to be distributed at all appropriate venues.

Currently, the alcohol toolkit is limited to literate persons. Further evaluation of the effectiveness of the toolkit is required once it is distributed. This will require additional funding. Plans on how to gather data on the uptake of the toolkit and methods for assessing the effectiveness will need to be

considered. The alcohol toolkit is not a self-help book. It has been developed to provide education and awareness to individuals and communities. Toolkit 7 can function as a self-help tool although it also may require some guidance in application.

CONCLUSION

Addressing alcohol-related harm is an ongoing process. It is a challenge for health professionals across the globe, particularly when working with more isolated, lower socio-economic and less educated communities. It is even more challenging in communities where alcohol is a strong aspect of cultural practices. Simply developing and distributing the toolkit amongst the communities is not enough. There is a need for ongoing engagement and collaboration to assist with the uptake of this message and to ensure appropriate and effective utilization of the tools. Further programmes need to be implemented to develop the support and intervention opportunities available in these areas.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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ORIGINAL ARTICLE

Initial Trauma Database in a University Hospital in Malaysia

Affirul Chairil Ariffin[1], Mohamed Hajhamad[2], Firdaus Hayati[3*], Nornazirah Azizan[4], Zamri Zuhdi[2], Azlanudin Azman[2], Ikhwan Sani Mohamad[5], Hairol Othman[2], Razman Jarmin[2], Jae Gil Lee[6]

[1] Department of Surgery, Universiti Sains Islam Malaysia, Kuala Lumpur, Malaysia
[2] Department of Surgery, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
[3] Department of Surgery, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[4] Department of Pathobiology and Medical Diagnostic, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu,Sabah, Malaysia
[5] Department of Surgery, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia
[6] Department of Surgery, Yonsei University College of Medicine, Seoul, South Korea

*Corresponding author's email: firdaushayati@gmail.com

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ABSTRACT

Trauma is a major health problem in Malaysia. An understanding of the trauma epidemiology is important in developing a reliable trauma service. The aim of this study is to understand the pattern of trauma in our institution and to highlight the need for a dedicated trauma service. In this database, 142 cases were included. Majority were males (127, 89.4%). Most common injury types are motor vehicle accidents (87.3%) followed by falls (7.7%) and stabs (3.5%). Most Injury Severity Score (ISS) falls under moderate score with 38.7%. Mean Abbreviated Injury Score (AIS) was 3 with most involving the chest and 90% of the patients have injuries involving at least 2 regions. Average hospital length of stay (LOS) was 11.4 days ±11.5 SD; with most patients (71.8%) were discharged without permanent disability. The mortality rate was 9.2% with all having ISS>16. ISS found to be strongly related to longer hospital stay and worse outcome (0.59, $p < 0.0001$, 0.4, $p < 0.0001$). This data is equivalent to the compared registries from 4 different trauma centres. However, steps need to be taken to improve this database. In conclusion, this university hospital receives a reasonable load of trauma cases yearly which is equivalent with other trauma centres. The increasing trauma cases will benefit from an implementation of a dedicated trauma service. This trauma database needs more depth in its elements and better data handling to ensure a quality and complete registry.

INTRODUCTION

Trauma remains one of the major causes of death worldwide. It causes a significant morbidity and mortality especially among

young adults. With the rise of urbanization and modernization, trauma cases are expected to rapidly increase. World Health Organization (WHO) has concluded that trauma is a cause for 11% mortality annually[1]. Countries with established trauma systems with designated trauma centres such as in United States, Australia and New Zealand have proved that a dedicated trauma organization and systems works well with positive effect in improving patients' outcome[2, 3, 4].

However, in most developing countries such as Malaysia, we rely on the trauma team activation approach which consists of general surgeons, emergency physicians and other supportive departments. Although it is a reasonable strategy approaching trauma cases, but the efficiency seems decreasing. Issues such as delayed consultations and referrals, missed findings and unreasonable investigation request via phone calls are just a few. This is attributed to the time constraint of the on-duty subspecialty physicians who must juggle between elective cases and clinic commitments. There is no analysis ever done looking at the outcome of this approach. We hope this article will show the needed evidence for a dedicated trauma services implementation.

In developing a trauma services and system, trauma registry is one of the major key components. The implementation of trauma registries in developed countries enables them to promote improvement of patient care, mortality and final outcomes[5]. It also plays a large role in prevention and quality assessment. However, articles on active trauma registries among developing countries are scarce and limited. Malaysia trauma system is in its nascent stage with no established national trauma database. The data collection and maintenance posed a challenged with limited trauma centres and limited funding of the registries. Other problem encountered during data collection is missing and incomplete data. This missing data presents a challenge when standardized registries are required as a benchmark. The objective of this study is to share preliminary trauma data collected in our university hospital and identify the weakness with optimism to improve for future collection.

MATERIALS AND METHODS

This study is a retrospective data collection from 2011 – 2013. The collection of trauma data was performed in Universiti Kebangsaan Malaysia Medical Centre (UKMMC), one of the university hospitals that serves as a tertiary centre in Kuala Lumpur, Malaysia. The figures were amassed from the trauma census kept by surgery, emergency and trauma department and intensive care unit. It consists of polytrauma patients and trauma cases presented under general surgery unit only. Pure neurosurgery and orthopaedic trauma cases were not included in the analysis due to incomplete and missing data.

The data was collected in a modified excel sheet with designated elements. Data elements collected include the demographics (gender, age, ethnic, and trauma type), time and day of injury and hospital presentation. Other parameters include the Injury Severity Score (ISS), management provided, the length of stay, the survival and difference in weekdays and weekends admissions and outcome. The Injury Severity Score (ISS) was calculated manually based on the Abbreviated Injury Scale (AIS) values[6, 7]. The data was calculated using mean and percentages. Pearson's correlation was used to determine the association between the Injury Severity Score (ISS), length of stay and outcomes.

RESULTS

There were 142 patients presented to our institution in recorded year (Table 1). Males were predominant with 89.4%. Trauma cases were common among the two major ethnics in Malaysia, Malay and Chinese with 41.5% and 39.4% respectively. The majority proportion of injury occurs within 15 to 59-year-old with 86.7% while the remaining patients occurs in 60 to 74-year-old and more than 74-year-old with each 7.1% and 5.6% respectively. We only see one paediatric trauma in our registry.

Table 1 Demographic data (*n* = 142)

Variables		Frequency (%)
Age group (years)		
	0 – 14	1 (0.6)
	15 – 59	123 (86.7)
	60 – 74	10 (7.1)
	>74	8 (5.6)
Gender		
	Male	127 (89.4)
	Female	15 (10.6)
Ethnicity		
	Malay	59 (41.5)
	Chinese	56 (39.4)
	Indian	14 (9.9)
	Others	13 (9.2)

Motor vehicle accident (MVA) remains the major cause for trauma in our institution with 87.3% (Table 2). Other cause of trauma was fall with 7.7%. Penetrating trauma was low in our data with 3.5% had stab wound and only one presented with gunshot wound. Presentation of trauma cases were more during the weekdays compared to weekends with 63.4% and 36.6% respectively. There was no difference in the time of presentation. Most patients present with more than one regional injury. There were total of 238 injuries for 142 patients with more than 90% have at least 2 different regions of injuries. The head and chest regions were the most involved with 23.5% and 33.1% respectively.

Table 2 Trauma type and presentation detail

Variables		Frequency (%)
Trauma type		
	Motor vehicle accident	124 (87.3)
	Fall	11 (7.7)
	Stab injury	5 (3.5)
	Gunshot	1 (0.7)
	Assault	1 (0.7)
Presentation day		
	Weekdays	90 (63.4)
	Weekends and holidays	52 (36.6)
Presentation time		
	Day (07:00 a.m. – 07:00 p.m.)	77 (54.2)
	Night (07:00 p.m. – 07:00 a.m.)	65 (45.8)

The mean AIS score is 3 with the majority involving the chest. There were significant numbers of AIS score of more than 5 which mostly involving the head and neck region. The mean ISS score was 18. Most of the patients in the registry are designated under ISS 9 – 15 (38.7%) followed by ISS ≥ 16 with 22.5%. A total of 32.4% of patients fall under critical ISS > 25 (Table 3). There were 10 deaths within the registry with all having ISS ≥ 16. All 10 mortalities involved the head region. Patients undergoing major intervention had longer length of stay (19.3 days) compared to both in the conservative and minor intervention

group (4.5 days and 7.8 days respectively). The statistical analysis using Pearson's correlation shows a strong association between ISS and length of stay (0.40, $p < 0.0001$, 95% CI 0.25 to 0.53) and final outcomes (0.59, $p < 0.0001$, 95% CI 0.47 to 0.69) (Table 4). The outcomes were shown to be better in patients with ISS ≤ 16, in which ISS was inversely related to length of stay and final outcomes.

Table 3 Severity assessment, length of stay and outcomes

Variables		Frequency (%)
Injury severity score		
	Minor (1 – 8)	9 (6.3)
	Moderate (9 – 15)	55 (38.7)
	Serious (16 – 24)	32 (22.5)
	Severe (25 – 49)	42 (29.6)
	Critical (50 – 74)	4 (2.8)
	Maximum (75)	0 (0)
Management		
	Conservative only	45 (31.7)
	Minimal intervention	38 (26.8)
	Major surgical intervention	58 (40.8)
	Referral to other centre	1 (0.7)
Length of stay		**Days**
	Conservative only	4.5
	Minimal intervention	7.8
	Major intervention	19.3
Final outcome		
	Discharge, no disability	11 (7.7)
	Discharge, non-permanent disability	102 (71.8)
	Discharge, permanent disability	16 (11.3)
	Death	13 (9.2)

Table 4 Correlation between ISS, length of stay and final outcomes

Variables	*p*-value	*r**	95% CI	
			Lower	**Upper**
Length of stay	<0.0001	0.59	0.47	0.69
Final outcomes	<0.0001	0.40	0.25	0.53

*Pearson's correlation

DISCUSSION

Trauma system has been shown to significantly improve the mortality rates in most developed countries. The establishment of working trauma systems requires meticulous planning, massive funding, appropriate government support and stringent policies. Despite its necessity is being argued previously but it has proven to be effective and reliable[6]. However, not every country is able to have such designation due to the lack of trauma system, integration of emergency services and source of funding[8].

The objective of this article is to share our trauma data in one of the tertiary university hospitals in Klang Valley, Malaysia. Our hospital is one of the 10 major hospitals in the city centre vicinity. Despite having the resources

and facilities, we are still lacking a dedicated trauma services within our institution. This may be attributed due to the lack of interest in trauma care among specialist, absence of a trauma surgeons and no appropriate support and funding from the governing body. Trauma cases in our institution are currently managed by a two-tiered trauma team activation consists of experts from multiple disciplines such as emergency physician, general surgery and other specialty unit. The activation of specialty depends on the type of injuries presented. This system is implemented in most countries which are yet to have trauma centres. It has previously shown to be reliable and effective[9]. However, the protocol and implementation vary among centres with no standardized managements.

This does not mean a trauma team response is not without any difficulties. With the advance in technology and new management in treating complex cases, most of the time is dedicated to non-trauma and elective works. These surgeons have found difficulty to divide equally their time between their specialty cases on top of dealing with occasional trauma cases. As an alternative, a dedicated trauma services could be started to cater the increasing trauma patients. There is strong evidence to suggest the implementation of a dedicated trauma services improves the patients' outcome. Few studies have shown the effectiveness of a dedicated trauma surgeon and trauma and critical care services in improving the survival outcome among trauma patients[10, 11]. More interestingly, a study done in Australia has showed small but significant reduction of 8% of mortality in severely injured patients[12]. We hope our data will emphasize the need for such services in our institution.

Another important concept in a trauma system is keeping a good trauma registry. This is important in quality improvement of trauma care[13]. Developed countries with established trauma system has been using trauma registries for in-house quality control and directing government policies[14]. Nevertheless, to develop a trauma registry, few setbacks need to be considered. Issues such as data collection, appropriateness of the collected elements, the ability to monitor and funding are just a tip of an iceberg in its development[15, 16].

Our centre is still far from developing a proper registry. However, an alternative to this now is compilation of trauma data based on the hospital admission and medical records. Majority of the data was collected using elements from another proposed trauma data registry and keyed into a modified Microsoft excel sheet.

Our institute received a reasonable load of trauma cases per year although this data does not include pure neurosurgery and orthopaedic trauma. A traffic accident was the major cause of trauma cases in our data. A total of 55% of patients presented to us had ISS more than 15. This signifies a high volume of cases with severe injuries. We compare ours with recent data from four trauma centres and their respective registries. Our data is equivalent with most of the registries in terms of cases presentation and severity assessment[17, 18, 19, 20]. The type of injuries encountered in most trauma centre is traffic accident except for Byun CS et al. (2015) whereby fall is predominant. However, our mortality is higher than Hasler RM et al. (2014)[14] and Byun CS et al. (2015)[21]. On the other hand, our mortality is similar with the data from the trauma centre in Europe. Though now mortality alone cannot be the measure of a trauma system success but is it a simple method to evaluate using a basic trauma database such as our institution[21].

Looking at the elements captured in the registries, we can conclude from the comparison table that most demographic data were similar. ISS is recorded consistently in all registries although the categorization was varied. However, elements used in the calculation Revised Trauma Score (RTS) and Glasgow Coma scale were not consistently recorded as per our database. This may be

attributed to the different objective and priority of each registries data handlers. If we compare with established trauma registries such as National Trauma Databank, Germany trauma registry, Korean National Trauma Databank, Australia and New Zealand trauma data registries and UK Trauma Audit and Research Network (TARN), our databank is lacking significant elements which include vital signs, Glasgow Coma Scale (GCS), prehospital data, arrival, admission and therapy timing, and RTS. All these elements are important to identify the pattern and weakness in each trauma systems[22, 23, 24]. Our database will need more depth and elements modification to make it more complete.

One of the major problems we encountered during data collection was missing and incomplete data. Because of this problem, we had to extract data only from general surgery, emergency and medical records. Pure neurosurgery and orthopaedic trauma cases had to be excluded due to the large number of missing and incomplete data. We also noted the problem in handling and computing data which is prone to error and repetitions when keyed in manually by specialists, residents and junior staff. This may be due to the miscommunications and limited time.

Our trauma database is a modest effort with an aim to identify the pattern of trauma cases using the available data to support our intention in developing a dedicated trauma service. Having said that, a more thorough and systematic approach should be taken to improve the database. This include optimizing data collection method, training of a dedicated personnel, having a better data capturing software, involvement of appropriate authority and ensuring flow of funding. Although there is no standard software or parameters list but most registry include the basic demographics, ward related information, AIS and any population specific information from their epidemiology studies.

We have identified few limitations of this study. Firstly, this is a retrospective data in a single tertiary university hospital. Secondly, exclusion of missing and incomplete data might cause inaccurate representation within the trauma scoring. The exclusion of pure neurosurgery and orthopaedic cases also might conceal the true amount of trauma cases presented to our institution. Thirdly, the wide variation of certain parameters such as demographics and injuries type cause inaccurate analysis hence the data may not be representative of a true cause of morbidity and mortality. Finally, we do acknowledge a possibility of more data loss due to lack of software or dedicated personnel for data handling and capturing.

CONCLUSION

The available data clearly suggests the need for a dedicated trauma services or at least a more stringent trauma protocol which encompasses all departments. Steps should be taken to modify this data compilation and organization to ensure more quality and reliable data collection.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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ORIGINAL ARTICLE

The Effects of Antipsychotic Drugs (Olanzapine and Risperidone) on Body Weight, Body Fat Percentage and Lipid Profiles of Patients with Psychotic Illness

Geo Allen George[1], Aza Sherin Yusuff[2], Wendy Shoesmith[2], M. Tanveer Hossain Parash[3]

[1] Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah, Malaysia
[2] Department of Community and Family Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[3] Department of Biomedical Science and Therapeutics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: geoallengeorge@gmail.com

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ABSTRACT

Approximately 50% patients with psychotic illnesses on antipsychotic drugs have an increased risk of obesity. This study aimed to determine changes in body weight, body fat percentage and lipid profiles and to stress the importance of early nutrition intervention in the management of psychotic illness patient treated with antipsychotic drugs. This is a prospective longitudinal study conducted for 3 months in Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah. A total of 150 patients with Diagnostic and Statistical Manual IV (DSM-IV) diagnosis of psychotic illness (either Olanzapine or Risperidone only at any dosage) first started or restarted after a treatment gap of at least 6 months were recruited. Weight, height and body fat percentage were measured using Bioelectrical Impedance Analysis (BIA) (Model Omron HBF-375) and blood fasting lipid test were taken from the point of starting medication for 12 weeks. Data were analysed using repeated measures of ANOVA for statistical method. All variables showed significant mean differences ($p < 0.05$) in increasing pattern throughout the 12 weeks of treatment. However, the total cholesterol of risperidone patients had no significant mean difference from initial to week 6 ($p = 0.282$). It was proven that there was increase in body weight, body fat percentage and lipid profiles among patients on olanzapine and risperidone. The limitation of this study might relate to the drugs' dosage and method used in assessing the body composition. It is suggested that early nutrition intervention is needed to control unnecessary gain of weight, body fat and lipid profiles in the management of patient with psychotic illnesses.

INTRODUCTION

The common treatment given to patients with psychosis illness is antipsychotic drugs (APDs). Antipsychotic drugs have two generations, namely the "first-generation" or conventional and the "second-generation" or atypical antipsychotic. Atypical antipsychotics are preferable over conventional antipsychotics[1, 2, 3]. Among the atypical antipsychotics, Olanzapine is the intermediate D2 antagonist and Risperidone is the high D2 antagonist. However, other side effects such as induced weight gain have rapidly become more evident[4, 5, 6]. This is concerning since these weight gains have been proven to lead the patients into exhibiting obesity[7, 8, 9]. Antipsychotic drugs (olanzapine and risperidone) are the most common APDs that prescribed in Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah according to the pharmacy unit.

DSM-IV defines psychotic illness as a clinically significant behavioural or psychological syndrome or pattern that occurs in an individual. It is associated with present distress, disability or with a significantly increased risk of suffering death, pain, or an important loss of freedom. According to National Health and Morbidity Survey 2015, in Malaysia, 29.2% adults and 12.1% children aged 5 to 15 are diagnosed with mental illness[10]. In East Malaysia, Sabah and Sarawak, there is lack of study that that could provide information on the prevalence rate of mental illness among residents in Sabah[11].

Many studies have been carried out to show the relationship between the consumption of antipsychotic drugs and obesity among patients with psychotic illnesses. Despite its low prevalence, psychosis illness can be an economic burden to a country, especially developing country[12, 13]. Malaysian doctors have been urged to provide these people with treatments and solution[14]. These treatments include the usage of APDs, whether in long term or short term. This, unfortunately, only increases the prevalence of obesity in Malaysia if the usage goes unmanaged.

This study aimed to determine the changes in anthropometric measurement, body composition as well as blood lipid profile among patients treated with olanzapine and risperidone. This study contributes as an empirical research. It provides an insight for future researchers to understand the importance of early nutrition intervention in the management of psychotic illness patients. This study could further explore how APDs can affect the anthropometric measurement and body fat percentage of patients. Since APDs are known to induce weight gain in most psychotic patients, the potential of inducing weight gain between Olanzapine and Risperidone is investigated. Thus, the objectives of the study were to analyse the changes in body composition among the patients when treated with Olanzapine and Risperidone.

MATERIALS AND METHODS

This study was conducted between 2015 and 2017 in terms of recruitment of patients and each eligible patient was following up for 3 months for this study at the Hospital Mesra Bukit Padang. This prospective longitudinal study was conducted over a period of three months involving 150 patients (76 males and 74 females). The number of subjects was calculated based on GLIMMPSE (General Linear Multivariate Model Power)[15]. The patients were aged between 18 and 45 years old diagnosed with psychotic illness based on the DSM-IV diagnostic criteria. Their treatment started with either Olanzapine (5 – 30 mg per day) or Risperidone (0.5 – 6 mg per day) which was assigned randomly according to the patients' medical condition and patients were experiencing either their first episode of psychosis or had not taken antipsychotic drugs in the last six months. The patients who were diagnosed with drug induced psychosis, affective disorders and having other medical problems that can affect the lipid profile or body fat composition, including diabetes, hyperlipidaemia and other endocrine disorders, on other medication which affect

the lipid profile or body fat composition (e.g. statins) and have an abnormal level of total cholesterol (more than 5.7 mmol/l), and TG (more than 2.3 mmol/l) and with a BMI of more 24.9 kg/m^2 and in Overweight and Obese range[2, 3, 4] were excluded from the study.

The data collection was approved by the National Medical Research Registry (NMRR-15-1006-26514) and all patients provided written informed consent before participating in this study. Opinion from professionals such as psychiatrists and medical officers will be considered to determine the ability of patient to give consent. The data will only be taken after consent given by the patient.

Information on patients' demographic data and current medications were obtained from their medical records. The researcher obtained access for patients' medical records as a health professional in the hospital. Patients' height was determined without shoes on a portable stadiometer with the Frankfort plane parallel to the floor according to National Health and Nutrition Examination Survey (NHANES) The head is in the Frankfort plane when the horizontal line from the ear canal to the lower border of the orbit of the eye is parallel to the floor and perpendicular to the vertical backboard. Body fat percentage was measured using the Body Fat Analyzer OMRON HBF 375 Weight Scale with correction for light indoor clothing. Fasting Lipid Profile (Total Cholesterol, triglycerides, high-density lipoprotein and low-density lipoprotein) of every patient in this study was obtained. All measurements mentioned were taken upon admission (Initial), week 6 and week 12.

The demographic characteristics of the patients were presented using frequencies, percentage and counts. To compare the main demographic and clinical characteristics among patients, repeated measures ANOVA was used to means of these variables at initial, week 6 and week 12. To further examine the relationship between APDs and the appetite of the patients, a chi-square analysis was performed. All these data were analysed using the Statistics-PC-software for Windows, Version 25.0.

RESULTS

There were 76 (51%) male patients and 74 (49%) female patients recruited for this research while 33 patients dropped out. The age distribution among the 150 recruited patients was normal with mean value of 32.65 $\pm$ 6.37 years old (Table 1).

Table 1 Socio-demographic characteristics of subjects (*n* = 150)

Variables		Overall (*n*)	Olanzapine *n* (%)	Risperidone *n* (%)
Gender	Male	76	44 (57.9)	32 (42.1)
	Female	74	37 (50.0)	37 (50.0)
Age	21 – 25	25	10 (40.0)	15 (60.0)
	26 – 30	41	24 (58.5)	17 (41.5)
	31 – 35	47	27 (57.4)	20 (42.6)
	36 – 40	11	7 (63.6)	4 (36.3)
	41 – 45	26	13 (50.0)	13 (50.0)

The research reported that 61 Olanzapine patients claimed to have increased appetite during the medication, 8 patients claimed decreased appetite while the remaining of 12 have no changes in appetite. While for Risperidone patients, 23 of them have increased appetite, 16 with decreased appetite and 30 of them with unchanged appetite (Figure 1).

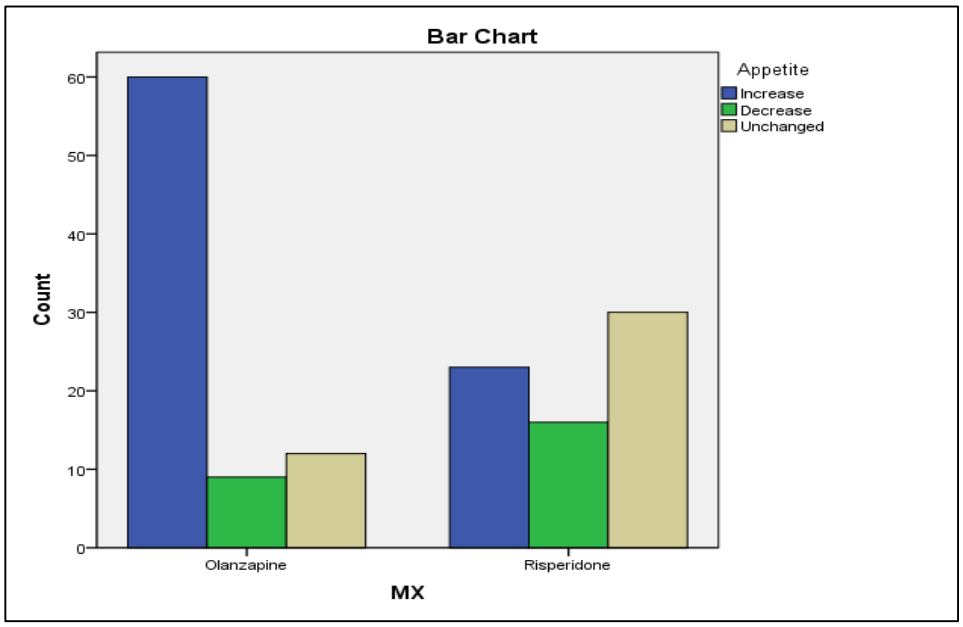

Figure 1 Distribution of appetite among patients taking Olanzapine and Risperidone

The means for Olanzapine and Risperidone patients' initial body weight were 56.11 ± 7.77 kg and 55.50 ± 8.00 kg respectively. For body fat, the means recorded for Olanzapine and Risperidone patients were 21.97 ± 4.26 % and 23.00 ± 4.54 % respectively while the results also revealed that the mean and standard deviation for waist were 28.59 ± 2.53 inch and 28.88 ± 2.88 inch respectively. The mean and standard deviation for hip were 32.77 ± 2.82 inch and 33.35 ± 2.75 inch respectively.

Table 2 Initial body composition among Olanzapine and Risperidone patients (*n* = 150)

Treatment	Variables	Minimum	Maximum	Mean	Std. Deviation
Olanzapine	Weight (kg)	36.0	72.0	56.11	7.77
	Body Fat (%)	12.7	29.0	21.97	4.26
	Waist (inch)	23.0	34.5	28.59	2.53
	Hip (inch)	27.0	41.0	32.77	2.82
Risperidone	Weight (kg)	38.0	73.0	55.50	8.00
	Body Fat (%)	14.2	33.8	23.00	4.54
	Waist (inch)	24.0	34.0	28.88	2.88
	Hip (inch)	25.0	38.0	33.35	2.75

The minimum triglycerides among patients is 0.04 and the maximum is 2.00. The mean for triglycerides cholesterol for Olanzapine and Risperidone patients is 1.16 with standard deviation of 0.29 and 1.13 ± 0.32. The minimum HDL among patients is 0.60 and the maximum is 1.90. The means for HDL of Olanzapine and Risperidone patients are 1.04 ± 0.22 and 1.05 ± 0.21 respectively. As for Low Density Lipoprotein (LDL), the minimum LDL among patients is 0.09 and the maximum is 4.10. The means of LDL for Olanzapine and Risperidone patients are 2.92 ± 0.75 and 2.88 ± 0.66 respectively. Table 3 illustrates that the minimum total cholesterol among patients is 3.00 and the maximum is 5.50. The means for total cholesterol are reported to be 4.29 ± 0.65 for Olanzapine and 4.29 ± 0.66 for Risperidone patients respectively. (Table 3).

Table 3 Initial Blood Lipid Profile among Olanzapine and Risperidone patients (*n* =150)

Treatment	Variables	Minimum	Maximum	Mean	Std. Deviation
Olanzapine	Triglycerides (mmol/L)	0.44	1.80	1.16	0.29
	HDL (mmol/L)	0.60	1.90	1.04	0.22
	LDL (mmol/L)	0.90	4.10	2.92	0.75
	Total Cholesterol (mmol/L)	3.00	5.30	4.29	0.65
Risperidone	Triglycerides (mmol/L)	0.04	2.00	1.13	0.32
	HDL (mmol/L)	0.60	1.70	1.05	0.21
	LDL (mmol/L)	1.50	4.00	2.88	0.66
	Total Cholesterol (mmol/L)	3.00	5.50	4.29	0.66

Table 4 and Table 5 summarize the mean and standard deviation for all the variables at initial, week 6 and week 12 for Olanzapine and Risperidone patients. The tables also reported that there were increasing patterns across the means of the dependent variables, except for HDL which displayed decreasing pattern from initial to week 6 and to week 12 for both Olanzapine and Risperidone patients. However, the results also revealed that there are no significant mean differences in HDL among patients treated with Olanzapine or Risperidone after week 6 (p = 0.143). In addition, the total cholesterol among Risperidone patients also show no significant mean difference from initial to Week 6 (p = 0.282). On the other hand, there is a significant mean difference from Week 6 to Week 12 which means the mean for total cholesterol increases only after week 6 of Olanzapine or Risperidone.

Table 4 BMI, weight, body fat at Initial, Week 6 and Week 12 for Olanzapine and Risperidone Patients (*n* = 150)

Variable	Medications	Mean Difference		Std. Error	95% Confidence Interval for Difference[a]	
				Lower Bound	Upper Bound	
BMI	Olanzapine	At week 6 vs initial	1.184*	.075	1.001	1.367
		At week 12 vs initial	2.347*	.118	2.059	2.634
		At week 12 vs at week 6	1.163*	.67	.999	1.327
	Risperidone	At week 6 vs initial	1.328*	.116	1.042	1.613
		At week 12 vs initial	2.626*	.155	2.245	3.007
		At week 12 vs at week 6	1.299	.080	1.102	1.495
Body weight (kg)	Olanzapine	At week 6 vs initial	3.069*	.367	2.172	3.966
		At week 12 vs initial	6.037*	.423	5.001	7.073
		At week 12 vs at week 6	2.968*	.167	2.559	3.377
	Risperidone	At week 6 vs initial	3.396*	.300	2.659	4.132
		At week 12 vs initial	6.641	.398	5.663	7.619
		At week 12 vs at week 6	3.245	.209	2.732	3.758
Body fat (%)	Olanzapine	At week 6 vs initial	1.820*	.163	1422	2.218
		At week 12 vs initial	3.473*	.220	2.936	4.010
		At week 12 vs at week 6	1.653*	.122	1.355	1.951
	Risperidone	At week 6 vs initial	1.777*	.201	1.282	2.271
		At week 12 vs initial	3.413*	.240	2.824	4.002
		At week 12 vs at week 6	1.636*	.127	1.324	1.948

* The mean difference is significant at the 0.05 level

Table 5 Blood Lipid Profile Parameters at Initial, Week 6 and Week 12 for Olanzapine and Risperidone Patients (n = 150)

Variable	Medications	Mean Difference		Std Error	95% Confidence Interval for Difference[a]	
				Lower Bound	Upper Bound	
Triglycerides (mmol/L)	Olanzapine	At week 6 vs initial	.314*	.040	.216	.411
		At week 12 vs initial	.482*	.043	.377	.588
		At week 12 vs at week 6	.168*	.022	.113	.223
	Risperidone	At week 6 vs initial	.233*	.034	.150	.317
		At week 12 vs initial	.339*	.048	.222	.456
		At week 12 vs at week 6	.106*	.037	.014	.197
Total Cholesterol (mmol/L)	Olanzapine	At week 6 vs initial	.560*	.063	.406	.715
		At week 12 vs initial	1.044*	.074	.864	1.225
		At week 12 vs at week 6	.484*	.048	.367	.601
	Risperidone	At week 6 vs initial	.806	.475	–.359	1.971
		At week 12 vs initial	1.254*	.473	.092	2.415
		At week 12 vs at week 6	.448*	.058	.306	.590
LDL (mmol/L)	Olanzapine	At week 6 vs initial	.478*	.060	.330	.625
		At week 12 vs initial	.953*	.068	.786	1.120
		At week 12 vs at week 6	.475*	.051	.352	.599
	Risperidone	At week 6 vs initial	.309*	.059	.164	.453
		At week 12 vs initial	.665*	.061	.516	.815
		At week 12 vs at week 6	.357*	.044	.249	.464
HDL (mmol/L)	Olanzapine	At week 6 vs initial	–.44*	.016	–.084	–.004
		At week 12 vs initial	–.091*	.020	–.141	–.042
		At week 12 vs at week 6	–.047*	.023	–.104	.010
	Risperidone	At week 6 vs initial	–.047*	.017	–.090	–.004
		At week 12 vs initial	–.064*	.018	–.108	–.021
		At week 12 vs at week 6	–.017	.017	–.060	.026

*The mean difference is significant at the 0.05 level

DISCUSSION

The weight gain can be seen through the mean differences of the patients' weight throughout the duration of the treatment. As revealed by the repeated measures ANOVA, there are significant mean differences for body weight of Olanzapine and Risperidone patients from initial to week 6 of treatment and week 6 to week 12 of treatment. This finding reaffirms the finding which indicated an association of APDs with weight gain among psychotic illness patients[16, 17]. Besides weight gain, that study also revealed differences in body composition among those that were induced by APDs compared to the control group[17].

From the statistical findings, all variables show significant mean differences in increasing pattern throughout the 12 weeks of treatment. However, the total cholesterol of Risperidone patients has no significant mean difference from initial to week 6 (p = 0.282). The results indicate the mean difference is only significant after the 6th week. The findings from repeated measures ANOVA indicate that there is no significant reduction HDL from week 6 to week 12 of treatment. The findings are also

consistent with a study where Risperidone was revealed to induce weight gain[16] among psychiatric patients with a mean weight gain of 4.3 kg after 12 weeks of treatment[18].

The patients are at risk of dyslipidaemia and cardiovascular as findings revealed increasing pattern for LDL and triglycerides from initial to week 12 while decreasing pattern of HDL from initial to week 6. The variation in patients' appetite does not help in predicting the APDs-induced body weight gain among the patients since some of the patients were reported to experience decreased appetite. It does however, shows that Olanzapine patients experienced higher increased appetite than the group that received Risperidone for their treatment[19].

The finding of this research seems to be in contrary with other studies that used a comparison of Olanzapine and Risperidone to determine their potential in inducing changes in weight gain and other body composition[20]. A study shows that Olanzapine induced more weight gain than Risperidone[21], however, for LDL, Risperidone seems to induce a significant change in LDL as compared to those treated with Olanzapine[22]. Lastly, although the result shows that patients prescribed Risperidone have higher weight gain compared to Olanzapine but there is no significant difference between the mean weight of Olanzapine and Risperidone, except on Low Density Lipoprotein (LDL) and Triglycerides.

Factors that could influence the side effect of APDs in inducing body weight gain among patients include its dosage and the demographic characteristics of patients[23]. Olanzapine has been known to be a dose-dependent drug, but the effects of Risperidone are less well known[24, 25, 26, 27]. Demographic characteristics such as age, gender and appetite were discussed to give a clearer picture on the confounding factors that could predict the body weight gain among patients[28].

The limitation of this study can be related to the drugs' dosage. In this study, the dosage of both Olanzapine and Risperidone were assigned by the clinicians according to the patients' needs. Hence, the dosage is not constant but varies with different patients. Next, there is a need to have control group, a control group is an essential element to allow the researchers to examine if the intended effects of the applied drugs are produced only by the drug[29].

CONCLUSION

It is proven that antipsychotic drugs induce changes in body weight, body fat percentage and lipid profiles among patients prescribed with Olanzapine and Risperidone. It is recommended that early nutrition intervention is crucial to control unnecessary weight, body fat and lipid profiles in the management of patient with psychotic illnesses that treated with antipsychotic drugs such as Olanzapine and Risperidone. Dietary counselling and monitoring of body weight and body fat may help to minimize the risk of obesity among psychotic patient on antipsychotic drugs.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this article.

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CASE REPORT

Abdominal Mass in the Puerperium: Challenges in Diagnosis

Sadesvaran Muniandy[1], Yvonne Teo Chiang Hoon[1], Aehtoosham Suleman[1], Prakash Doddaballapur Ramaiah[2*]

[1] Emergency and Trauma Department, Hospital Duchess of Kent, Sandakan, Sabah, Malaysia
[2] Department of Surgery, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email: drprakash@ums.edu.my

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post-partum, puerperium, abdominal mass, ovarian carcinoma, pregnant

ABSTRACT

Ovarian cancer is the fourth most common cancer among women in Peninsular Malaysia. Epithelial ovarian cancer accounts for 90% of all ovarian tumours. Herein, we present a rapidly growing ovarian tumour in a young female patient, following an uneventful vaginal delivery at home. We discuss on the challenges of making said diagnosis in a post-partum patient who presented with abdomen distension. A 19-year-old lady presented to the Emergency Department three days after spontaneous vaginal delivery at home. Her chief complaint was that of a rapidly progressive abdominal distension. Diagnostic and therapeutic emergency laparotomy were done, revealing a huge cystic ovarian mass. Histopathology reported a high grade, serous ovarian carcinoma. There are multiple causes for abdominal distension in post-partum women, however priority should be given into looking for gynaecological origin, given the changes in hormone. Sudden abdominal distension during post-partum period is rare and a systemic approach in its management is vital. There is, inarguably, a role of diagnostic and therapeutic laparotomy in this.

INTRODUCTION

According to the National Cancer Registry, ovarian cancer is the fourth most common cancer among women in Peninsular Malaysia, making up five per cent of all female cancer cases and the most malignant gynaecological malignancy[1]. Ovarian epithelial cancer is the most common form of ovarian cancer[2]. Epithelial ovarian cancer, accounts for 90% of

all ovarian tumour, is grouped into four major histological types; serous (70%), endometrioid (10 – 15%), clear cell (10%) and mucinous (3%)[1]. Herein, the authors present rapidly growing ovarian tumour in a young female patient following uneventful vaginal delivery at home. The authors discuss on the challenges of diagnosis of a patient presented with abdomen distension in post-partum period.

CASE PRESENTATION

A 19-year-old lady, para 1, non-Malaysian, presented to Emergency Department three days after spontaneous vaginal delivery at home with chief complaint of rapidly progressive abdominal distension. She delivered to a healthy baby at home, assisted by an untrained midwife. She did not have any proper antepartum follow-up during the pregnancy due to financial constraint. She denied any abdominal swelling prior to pregnancy and her abdomen enlarged appropriately during the 9 months period of pregnancy. Post-delivery, she developed abdomen distension, which increased in size within 3 days. Abdomen distension was massive till she started to have a pain and difficulty in breathing. She had bouts of vomiting with reduced oral intake after that. She has no similar symptoms prior to or during pregnancy. However, she still had a normal bowel opening and denied any urinary abnormality. She had a normal lochia and did not have any fever or constitutional symptoms. There was no family history of malignancy.

On examination, she was alert, pale, not jaundice and a febrile. She was tachypnoeia, as a result of diaphragm splinting. Otherwise, her vital signs were stable. Lungs were clear and heart sound was normal. Her abdomen was grossly distended, even larger than a term pregnant lady. Per abdomen examination revealed abdomen was distended, tensed, dull on percussion and presence of fluid thrills. The bowel sound was still present. Per rectal and per vaginal examination were normal. Abdomen radiograph shows generalised opacity, unable to visualize any intra-abdominal organ (Figure 1). Bedside ultrasound abdomen done showed large amount of ascites, obscuring the view of any organs or mass in abdomen

Figure 1 Abdominal radiograph showing generalised opacity, obscuring the pelvic bone

She was subsequent reviewed by the gynaecologist team and a provisional diagnosis of ovarian cyst was made based on acute onset history with likelihood of being ovarian origin cyst. She then underwent emergency laparotomy, revealing a huge cystic ovarian mass (Figure 2). Unfortunately, the mass was accidentally punctured intra-operatively during manipulation, draining 11 litres of haemoserous fluid (Figure 3). She remained stable intra-operatively. The histopathology result came back as high grade serous with lymphovascular involvement and disrupted capsule. The malignant cells had also microscopically extended to fallopian tube and omentum (Figure 4). The patient requires staging and subsequent chemotherapy. The patient was discharged in a well condition a week after that. Patient could not afford for tumour marker test. Unfortunately, the patient failed to turn up for her follow-up in clinic as she was unable to pay for the bill.

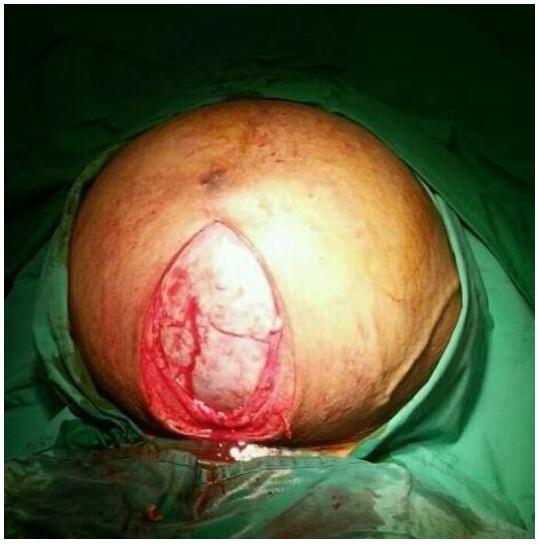


Figure 2 Taken intra operatively, showing the grossly distended abdomen

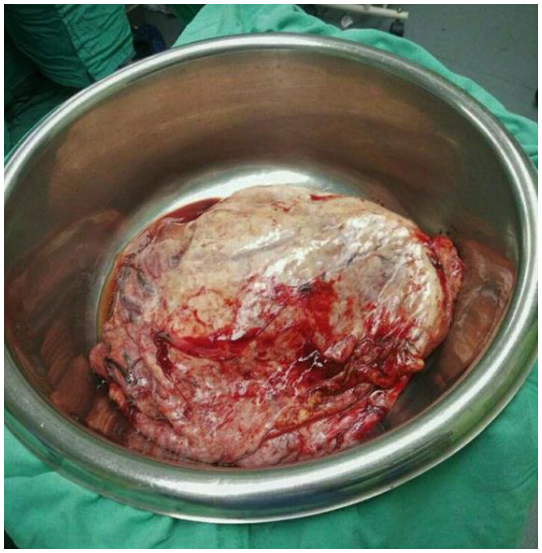
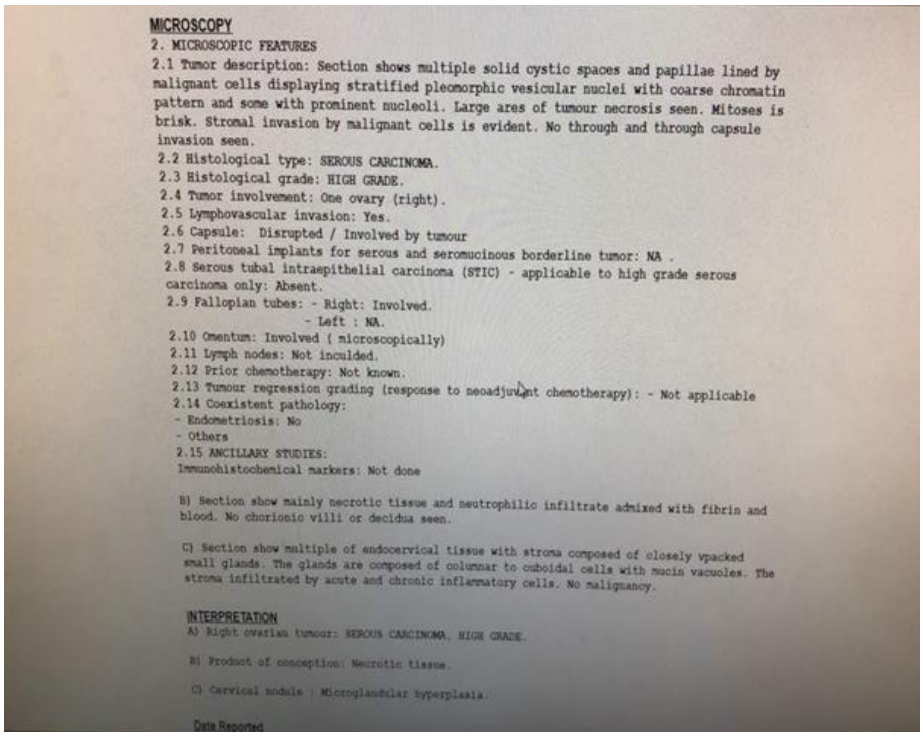


Figure 3 Showing the ruptured cyst, drained 11 litres of serous fluid



MICROSCOPY

2. MICROSCOPIC FEATURES

2.1 Tumor description: Section shows multiple solid cystic spaces and papillae lined by malignant cells displaying stratified pleomorphic vesicular nuclei with coarse chromatin pattern and some with prominent nucleoli. Large ares of tumour necrosis seen. Mitoses is brisk. Stromal invasion by malignant cells is evident. No through and through capsule invasion seen.

2.2 Histological type: SEROUS CARCINOMA.

2.3 Histological grade: HIGH GRADE.

2.4 Tumor involvement: One ovary (right).

2.5 Lymphovascular invasion: Yes.

2.6 Capsule: Disrupted / Involved by tumour

2.7 Peritoneal implants for serous and seromucinous borderline tumor: NA .

2.8 Serous tubal intraepithelial carcinoma (STIC) - applicable to high grade serous carcinoma only: Absent.

2.9 Fallopian tubes: - Right: Involved.
- Left : NA.

2.10 Omentum: Involved (microscopically)

2.11 Lymph nodes: Not included.

2.12 Prior chemotherapy: Not known.

2.13 Tumour regression grading (response to neoadjuvant chemotherapy): - Not applicable

2.14 Coexistent pathology:
- Endometriosis: No
- Others

2.15 ANCILLARY STUDIES:
Immunohistochemical markers: Not done

B) Section show mainly necrotic tissue and neutrophilic infiltrate admixed with fibrin and blood. No chorionic villi or decidua seen.

C) Section show multiple of endocervical tissue with stroma composed of closely vpacked small glands. The glands are composed of columnar to cuboidal cells with mucin vacuoles. The stroma infiltrated by acute and chronic inflammatory cells. No malignancy.

INTERPRETATION

A) Right ovarian tumour: SEROUS CARCINOMA, HIGH GRADE.

B) Product of conception: Necrotic tissue.

C) Cervical nodule : Microglandular hyperplasia.

Date Reported

Figure 4 Histological report

DISCUSSION

Postpartum period is loosely defined as the period immediately following childbirth. The term puerperium extends further and refers to the first 6 weeks after delivery, during which the reproductive organs are returning to their normal condition following labour and delivery.

A dramatic decrease in the concentrations of many hormones occurs in women after labour. Two main steroid hormones that have been maintaining pregnancy are oestrogens and progesterone. Since these hormones are predominantly produced by the placenta, progesterone and estradiol decrease rapidly to pre-pregnant concentrations within 72 hours after delivery, as these hormones are predominantly produced by the feto-placental unit and is no longer producing them.

This patient was in day three post-partum and urine pregnancy test was negative. She did not have any per vaginal bleeding and bedside ultrasound could not localize any foetus either. A differential diagnosis would be an ovarian cyst, in view of grossly distended abdomen. There are reported case of large ovarian cyst misdiagnosed as ascites[2]. The best diagnosis that fit into the patient was ovarian cyst as it fits most of the history. An ovarian cyst is a sac filled with liquid or semi-liquid material that arises in an ovary. Most of ovarian cyst patients are asymptomatic. As ovarian cyst being asymptomatic, it is therefore commonly found during ultrasound.

Another differential diagnosis that need to be considered is HELLP syndrome with complicated with ascites. El-Agwany et al. (2015) reported that a patient with normotensive HELLP syndrome developed ascites post-partum. The patient was managed conservatively and abdominal swelling resolved. Massive ascites is defined as accumulation of more than 2 litres of fluid in the peritoneum. If untreated, it can lead to respiratory compromise. This patient came with diffuse abdominal distension which suggestive of gross ascites. Fortunately, her blood pressure was normal, and all her blood parameters did not point towards HELLP syndrome[3].

Among many other gynaecological malignancy, ovarian tumour is the number one killer. However, ovarian cancer is only three per cent of all cancer in women[4]. However, the history of abdominal distension was too brief to support towards this diagnosis. Another possible diagnosis of the abdominal distension could be intestinal obstruction. However, patient was still able to pass flatus and she had no vomiting. Besides that, her abdominal radiography does not show any dilated bowel.

Bladder ascites should also be considered as part of the differential diagnosis of abdominal distension in a puerperium patient. Pandit V et al. (2016) reported an interesting case of a post-partum lady presented with ascites and oliguria. She was initially treated for urinary tract infection twice before suffering from ruptured urinary bladder with leakage of urine into the peritoneum[5]. It is commonly associated with uterine rupture and increase risk with delivery conducted by untrained personnel. CT cystogram is the best diagnostic modality to confirm the diagnosis, which is unavailable in our centre.

Ovarian torsion is the fifth most common gynaecological emergency with a reported prevalence of 2.5 – 7.4% in patients undergoing emergency surgery for acute pelvic pain[6]. The diagnosis of ovarian torsion during puerperium is often missed due to non-specific symptoms and uncommon objective finding[7]. Ovarian mass, be it malignant or benign must be considered as part of the differential diagnosis for women of any age, especially during post-partum period[8]. Presentation of ovarian torsion and other puerperium-related disorder is quite similar.

Abdominal distension after delivery can be due to pneumo-peritoneum too. There is another reported case of a patient, day 6 post-partum, presented with abdominal swelling and severe pain. She was subsequently diagnosed as pneumoperitoneum evident by air under diaphragm. It is a well described fact that in women, air may travel up through the genital tract and enter the peritoneal cavity, resulting in pneumoperitoneum[9].

There is a case reported about a puerperal patient presented with abdomen pain and was treated as renal colic initially. Patient was not responding to initial treatment; therefore ultrasound was ordered, which revealed ovarian mass. Diagnosis was altered to ovarian torsion[8].

Imaging is frequently used in the diagnosis of an acute abdomen. Ultrasound has become the routine bedside examination to rule out potential pelvic pathologies. Emergency physicians are suggested to master gynaecological-based ultrasound, as gynaecology emergencies are picked up by bedside ultrasound. Ovarian torsion during pregnancy and puerperium is a challenging diagnosis for emergency physicians due to largely the non-specific signs and symptoms involved[7]. A scan performed by senior gynaecologist or radiologist would make a huge difference. However, there are cases reported where ovarian malignant tumour could not be identified during routine antenatal ultrasound at 10, 12, 15 and 20 weeks of gestation[10]. The study did not specify who did the ultrasound. Our Malaysian policy for maternal and child health has stated that antenatal scan to be performed at time of booking, 16 and 32 weeks. Our patient did not go for any antenatal check-up; therefore, no scan was done for her earlier. There was limitation in doing ultrasound for her on presentation in Emergency Department as only fluid could be seen and not the other intra-abdominal or pelvic organs.

At the time of discharge, patient was informed about the intra-operative findings and that the mass is likely to be malignant. She was given an appointment. According to the histopathology reports, the patient required staging and subsequent chemotherapy. This is not surprising as most cases of high-

grade serous ovarian cancer are diagnosed at advance stages, when the tumour has already metastases[1]. The final result could not be explained to patient as she had lost from follow-up and was not contactable. As an unregistered patient and from poor social economy background, patient was unlikely to be affordable for expensive treatment. This can lead to further deterioration of her clinical condition.

CONCLUSION

A patient presenting with abdomen distension can lead to variety of possible diagnosis especially when presented with acute symptoms. A proper examination is always the best in ruling out differential diagnosis. Bedside ultrasound especially in the hand of an expert helps to diagnose patients in emergency setting.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Ultrasound Subcostal Approach Transversus Abdominis Plane Block in Morbidly Obese Patient

Nelbon bin Giloi[1*], Constance Liew Sat Lin[2], Alvin Oliver Payus[2], Rhanye Mac Guad[3], Chandrika Murugaiah[3], May Zaw Soe[4], Shaila Kabir[2], Soong Shui Fun[5], Symeon Mandrinos[6]

[1] Department of Community and Family Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[2] Department of Medicine Based Discipline, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[3] Department of Biomedical Science and Therapeutic, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[4] Department of Reproductive Health, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[5] Department of Nursing, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[6] Swinburne University of Technology, Sarawak Campus

*Corresponding author's email: nelbon.giloi@ums.edu.my

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obesity, postoperative pain, laparoscopic cholecystectomy, ultrasound

ABSTRACT

As general population of obese patients in Malaysia rapidly increases, more obese patients are requiring anaesthesia for various operative procedures. Obesity is associated with anatomical and physiological differences and co-morbidities that influence on the choices of anaesthesia care. A surgical case with general anaesthesia is used as a basis of discussion. A 37-year-old female, history of untreated hypertension and gastro-oesophageal reflux disease (GORD), BMI of 41 admitted for laparoscopic cholecystectomy for symptomatic cholelithiasis under general anaesthesia. She presented with pain at the upper right abdomen and associated with bloated abdomen, nausea and vomiting after intake of meals. General anaesthesia and right ultrasound-guided transversus abdominis plane (TAP) block for abdominal wall blocks via subcostal approach was performed. Operation was removal gallstones in the common bile duct via laparoscopic approach. Post-operation patient was extubated successfully. She was prescribed paracetamol 1g 4 hourly and started on fentanyl patient-controlled analgesia (PCA) for next 2 days. In this case report, there is the description of the application of TAP block which when used in obese abdominal surgical procedure, can provide excellent postoperative pain relief, early mobilization and recovery.

INTRODUCTION

World Health Organization (WHO) reported 650 million adults worldwide have a BMI > 30kg/m^2 and are thus classified as obese. With an increasing obese population, it is not surprising that the number of obese

patients being anaesthetised is also rising[1]. It is well known that obesity is a risk factor for many health conditions such as ischaemic heart disease and respiratory problems[2]. Anaesthesiologists and surgeons should be aware of this high-risk candidate case for operation under a well-equipped operating theatre for difficult intubation and impending potential difficult resuscitation. Obesity is involving both respiratory and cardiovascular systems and overall metabolic functions of liver, kidneys and pituitary gland and, therefore, multidisciplinary assessment to evaluate is required. Early anaesthesia clinic visit is consulted to assess the pain and provide adequate pain relief before operation[3].

CASE PRESENTATION

A 37-year-old female with a BMI of 41 (height 1.68 m, weight 113 kg) electively required laparoscopic cholecystectomy for symptomatic cholelithiasis under general anaesthesia. Her co-existing co-morbidities consisted GORD and untreated hypertension. She had no known any food or drug allergies. She had 2 previous caesarean sections. Further history revealed witnessed snoring, multiple episodes of awakening from sleep, and daytime somnolence. Her STOP-Bang score was 5 with high possibility of moderate/severe obstructive sleep apnoea (OSA)[4]**.** Due to lack of equipment and facility, sleep study could not be done to evaluate the degree of sleep deficiency and apnoea/hypopnoea index (AHI).

After securing 18G branula for intravenous access on the dorsum of the right hand, vital parameters blood pressure, pulse, oxygen saturation and ECG were monitored on the left hand. She was in ramp position with multiple pillows placed from back of both shoulders to head to facilitate tracheal intubation. Preoxygenation 3 minutes with 100% oxygen, rapid sequence induction with Sellick manoeuvre were applied and administration of intravenous fentanyl 100 mcg, propofol 100 mg, and suxamethonium 100 mg. When the patient loss of consciousness, intubation was performed using C-MAC® video laryngoscope, a current and preferred method in obese patients[5]. The cricoid pressure was maintained until five consecutive end tidal carbon dioxide (ETCO2) readings were confirmed. The times to optimal glottis view and to securing the airway displayed on video laryngoscope screen, defined as the time lapsing holding the C-MAC laryngoscope to the best glottis exposition was 14 seconds with single attempt intubation. Endotracheal tube size 7.5 was anchored at 21 cm at lip level and auscultation of both basal and upper lungs confirmed equal air entry to both sides of the chest. The lowest arterial oxygen saturations were 93% and 95%. Anaesthesia was maintained with inhalational agent desflurane 6% in oxygen mixture air at 3 litres/min each and intermittent boluses of rocuronium 10 mg every 20 – 30 minutes. Invasive arterial line and 18G intravenous line ware inserted on the right hand. Mechanical ventilation settings were adjusted according volume-controlled mode at minimum respiratory rate of 15 per minute, minimum tidal volume of 6 ml per kg.

Right TAP blocks via subcostal approach was performed under sterile technique. A high frequency linear ultrasound probe was covered by a sterile plastic and placed perpendicular to the abdominal wall, directed parallel to the subcostal margin (Figure 1). An ultrasound needle of 100 to 150 mm was placed near the medial side of the ultrasound probe and the local anaesthetic was firstly deposited between transversus abdominis fascia and the rectus abdominis sheath, or between the rectus abdominis sheath and the posterior rectus sheath if transversus was not visible. Then needle was directed inferolaterally to deepen gradually in order to distend the transversus abdominis plane (Figure 2). Two injection points were to ensure that local anaesthetic was deposited adequately along the plane. In total of 30 ml of 0.5% ropivacaine was administered. Prophylaxis of post-operative nausea and vomiting (PONV) using intravenous dexamethasone 8 mg was administrated.

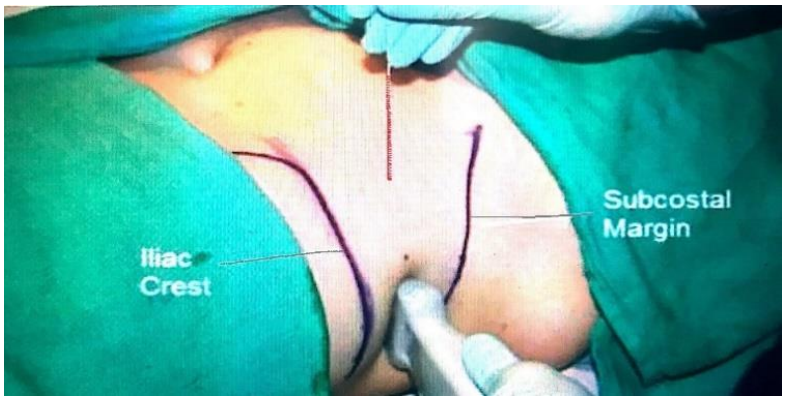

Figure 1 A high-frequency linear ultrasound probe was placed on the abdominal wall directed towards the costal margin as shown

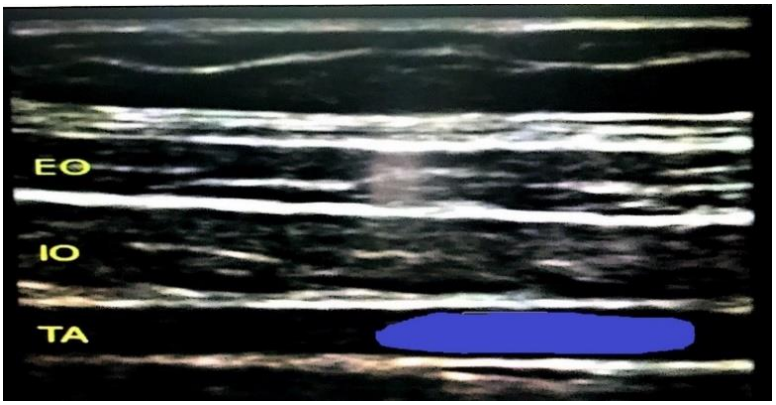

Figure 2 Illustration depicting the ideal placement of the local anaesthetic drug in blue coloured region (EO: external oblique muscle, IO: internal oblique muscle, TA: transversus abdominis muscle)

The surgery lasted for 168 mins. Estimated blood loss during the surgery was less than 500 ml. The entire operation lasted 2 hours 30 minutes, with no untoward events intra-operatively. Anaesthesia was reversed with injection 200 mg sugammadex and she was extubated successfully. She was on face mask with 3 litres per minute fresh gas flow for 40 minutes until her dizziness subsided at the recovery. She was started intravenous paracetamol 1 g 6 hourly, intravenous enoxaparin 40 mg 12 hourly and fentanyl PCA for 2 days by the acute pain service doctor. Her pain score was 2/10 scale in the ward, and she was able to breathe comfortable at rest and weaned of fentanyl PCA after 24 hours post-operation.

DISCUSSION

Morbid obesity has many detrimental effects on various body systems. It is frequently related to dyslipidaemia, diabetes, increased risk of myocardium ischemia, increased oxygen consumption, increased carbon dioxide production and predisposed to gallbladder diseases. The pharmacokinetics parameters in morbid obesity patients altered depending on volume of distribution (Vd), clearance (Cl) and protein binding and drug elimination pathways. These values can be deviated 20 – 40% in a morbidly obese patient.

Morbidly obese patients are well known at critical risk with regards to aspiration and upper airway obstruction following endotracheal tube removal post-operation. Prompt and fast reverse from anaesthesia

is needed for early return of cough reflex to protect the airway from aspiration and oesophageal regurgitation[6]. Thus, our preferred choice of induction agent and muscle relaxant were short and medium acting anaesthetic agents such as fentanyl, propofol, desflurane, rocuronium and sugammadex. Desflurane has the lowest lipid solubility compared with other inhalational agents in the market and is quickly eliminated from the various organs and systems irrespective of duration of use. Besides that, the haemodynamic parameters such as blood pressure, cerebral perfusion pression, pulse and cerebral oxygen consumption is less fluctuated, and that post-operative recovery was shorter duration and post-operative hypoxemia risk was reduced[7].

Sugammadex was chosen for our patient because sugammadex provides more effective and more secure recovery in comparison with neostigmine in morbidly obese patients[8]. The dose of sugammadex used is depending on the depth of neuromuscular block at the end of operation and the last dose of rocuronium served. The patient's neuromuscular block train of four (TOP) ratio was 0.5 and 200 mg sugammadex was administered and desflurane was stopped. Patient woke up in approximately 3 minutes and did not encounter any problem in the recovery phase as well as the post-operative follow-up.

TAP is a simple yet often overlooked peripheral block targeting the exit points the intercostal nerves of the anterior abdominal wall. The block has been proven to be effective adjunct post-operative pain relief for various gynaecologic and abdominal surgeries. The longstanding technique of identification of lumbar triangle of Petit followed by hearing 2 'pop' sounds indicates the first 'pop' sound represents the penetration of external oblique fascia followed by second 'pop' sound indicates the penetration internal oblique fascia that was used before the advance of ultrasound high-frequency linear probe. Both in-plane needle approach and short-axis approach nerve visualization techniques were able to access clearly the expansion site under the ultrasound scan and depth of deposition of local anaesthetic solution under the abdominal tissue. A success rate TAP block will be more predictable at approximately 70% and reduce complication rate by 20%[8].

A systematic review of the published literatures recognised a total of 7 randomized clinical trials (RCT) looking into the beneficial outcomes of TAP block on post-surgical pain, including 180 patients from total 364 patients who received TAP blockade during operation[9]. The surgical procedures included various bowel resection surgeries with a midline abdominal incision, caesarean delivery via the Pfannenstiel incision, gynaecological hysterectomy with a transverse abdominal wall incision, minor operations such as open appendectomy and laparoscopic cholecystectomy[9]. The outcomes compared were pain score at immediate post operation period, 24 hours post-operation and 48 hours post-operation period, the total amount of opioid requirement, the side effects of PONV, respiratory depression, drowsiness, and satisfaction score among the patients.

CONCLUSION

In general, the outcomes of TAP blocks in any gynaecologic and abdominal surgeries are very promising and various studies have proven significant reduction of opioid use and pain and subsequently opioid overuse or opioid intolerance such as sedation and PONV. In this case report, the application of TAP block was in obese abdominal surgical procedure. This caused an excellent postoperative pain relief, early mobilization and recovery. More works are necessary to elicit the outcomes of the previous studies in order to establish the use of TAP blocks extensively.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

A Rare Case of Synovial Osteochondromatosis of the Elbow

Loh Li Loong[1*], Wong Kai Ann[2], Zamzuri Zakaria@Mohamad[1]

[1] Department of Orthopaedic, Traumatology and Rehabilitation, Islamic International University Malaysia Medical Centre, Kuantan, Malaysia
[2] Department of Orthopaedic, Hospital Seberang Jaya, Penang, Malaysia

*Corresponding author's email: liloong85@yahoo.com

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ABSTRACT

Synovial osteochondromatosis is an unusual, rare and benign tumour. This disease is characteristically monoarticular, most commonly found in knee joint, however it is rarely found in the elbow. A 49-year-old Indian man presented to hospital with a 6-month history of pain, swelling, intermittent locking, loss of range of motion of right elbow and a considerable size of elbow with no recollection of associated trauma. Plain radiographs of right elbow showed numerous radiopaque round and oval loose bodies within the right elbow joints. Computer Tomographic (CT) scan showed multiple bony mass within the right elbow joint. Arthroscopic synovectomy, debridement, excisional biopsy and loose body removal combined with mini-arthrotomy of the right elbow was performed due to limited exposure for removal of larger loose bodies. Histopathological examination of the tissue sample is consistent with the diagnosis of synovial osteochondromatosis. The clinical and radiological evaluation at 6th month postoperatively showed marked reduction in the volume of the elbow, further improvement of elbow range of motion of this patient and the Mayo elbow performance score before surgery and at 6 months postoperative, with an increase from 50 to 80 points. Synovial osteochondromatosis of the joints is a rare condition. The signs and symptoms are not specific and may be suggestive of other pathology conditions. Arthroscopic synovectomy and removal of loose body is the standard operative procedure till today. However, combination of arthroscopy and mini-arthrotomy in cases of large loose bodies may provide a good clinical and functional outcome.

INTRODUCTION

Synovial osteochondromatosis is an independent disease which is unusual, rare, benign, chronic, and progressive metaplasia of the synovium of joints[1, 2], and may arise from tendon sheath or bursae. Synovial formation of cartilaginous or osteochondral bodies[3, 4] is the characteristic of synovial osteochondromatosis which are typically intra-articular or may be extra-articular[5]. The cartilaginous tissues undergo calcification and ossification producing multiple osteochondral nodules and the cause of the metaplasia is still unknown. In 1558, this disease was first described in the knee by Ambrose Paré[6] and later in 1813, Laennec reported that loose bodies within the joints arose from the subsynovial tissues[7]. Brodie confirmed that the loose bodies originated from synovium although he noted that it could arose outside the synovial membrane in some cases[8].

The disease is characteristically monoarticular, most cases involve the knee[1]. A case of synovial osteochondromatosis in the elbow was reported firstly in 1918 by Henderson[9], but it could involve in any other joints[1].

Synovial osteochondromatosis occurs either in primary or secondary form. High levels of BMP-2 and BMP-4 have been isolated from diseased synovium and free bodies although the molecular basis is still unclear[10]. Primary synovial osteochondromatosis is being described as the presence of ectopic cartilage in synovial tissue and as loose bodies in the joint cavity with or without calcification in the otherwise normal joint, and secondary synovial osteochondromatosis is a similar proliferative disorder of synovium in joints with degeneration of articular cartilage and subchondral bone often containing previous loose bodies that arose secondary to fracturing of the joint surface[11]. These two forms of synovial osteochondromatosis can be differentiated based on a histopathological examination of the surgically excised loose bodies[12].

We wish to review the clinical and surgical treatment options in a rare case of synovial osteochondromatosis of the elbow. Arthroscopic synovectomy and excision of loose bodies is the standard treatment of synovial osteochondromatosis till today. However due to the limitation of arthroscopic portal to remove the larger loose bodies, mini open arthrotomy was converted and this combination technique has never been never mentioned in any literatures till today and still provide a good clinical and functional outcome.

CASE PRESENTATION

A 49-year-old Indian man with underlying hypertension, hypercholesterolaemia presented to hospital with a 6-month history of pain, swelling, intermittent locking, loss of range of motion of right elbow and a considerable size of elbow with no recollection of associated trauma. Other joints appeared to be normal. The right elbow the lacked 15° of full extension and had 100° of flexion (Figure 1A, 1B, 1C).

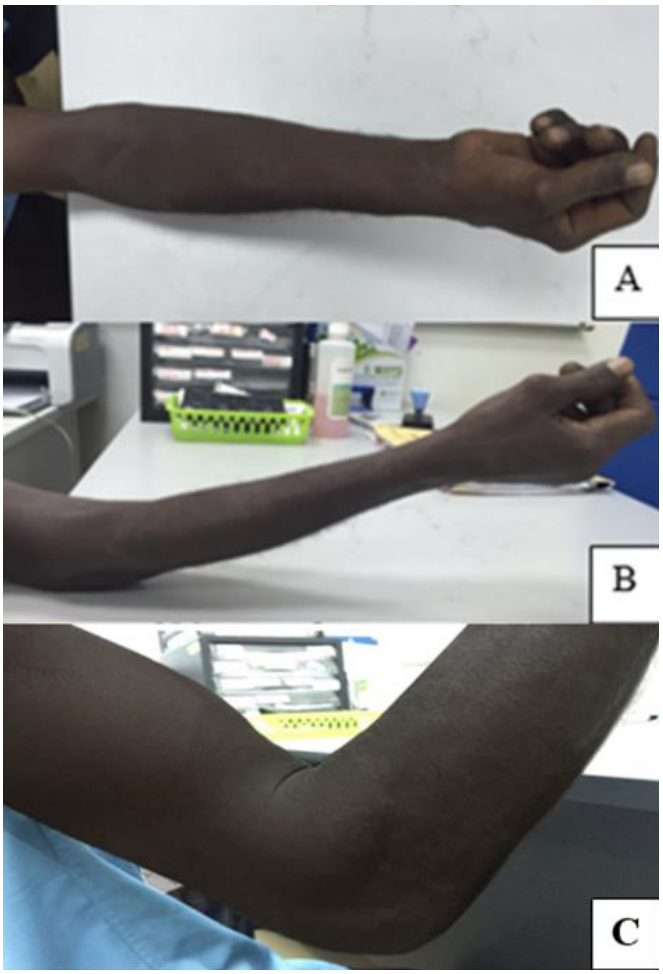

Figure 1 Figure 1A (anterior view), 1B (lateral view in extension) – right elbow lacked 15° of full extension, 1C (lateral view in flexion) – right elbow lacked 45° of full flexion

However, pronation and supination were substantially complete; crepitus was appreciated throughout elbow motion typically when the elbow was brought from flexion to extension and. No vascular or neurologic compression symptoms were observed. A plain radiographic showed numerous radiopaque round and oval, calcified loose bodies widespread throughout the right elbow joint. Multiple large loose bodies were seen within the coronoid fossa region (Figure 2A, 2B).

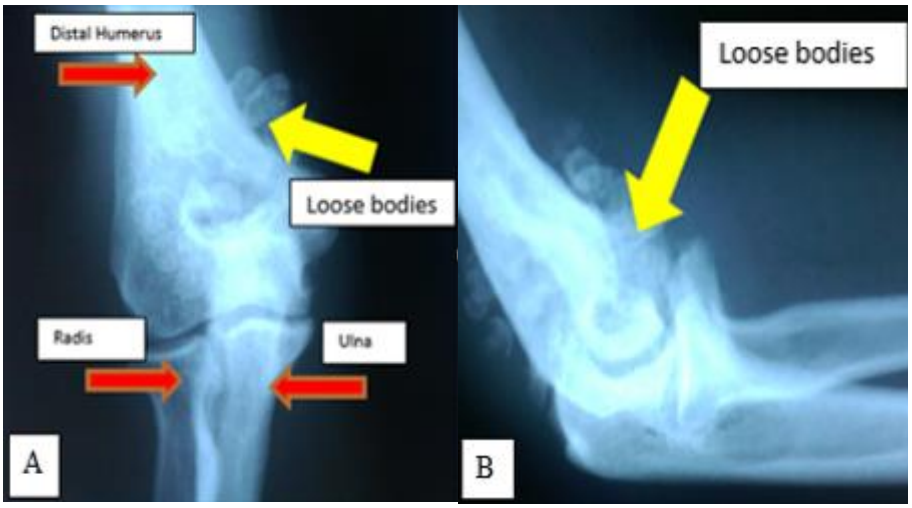

Figure 2 Figure 2A – anteroposterior view and 2B – lateral view. Plain radiographs of right elbow showed numerous radiopaque round and oval loose bodies within the right elbow joints. Note the large loose body within the coronoid fossa region.

CT scan showed multiple calcified nodules with a ring and arc patterns of mineralisation (central focus with peripheral calcification) surrounding the right elbow joint (Figure 3). These changes can be visible on plain radiographs, however they are better appreciated on CT scan. Diagnosis of synovial osteochondromatosis of the right elbow was made.

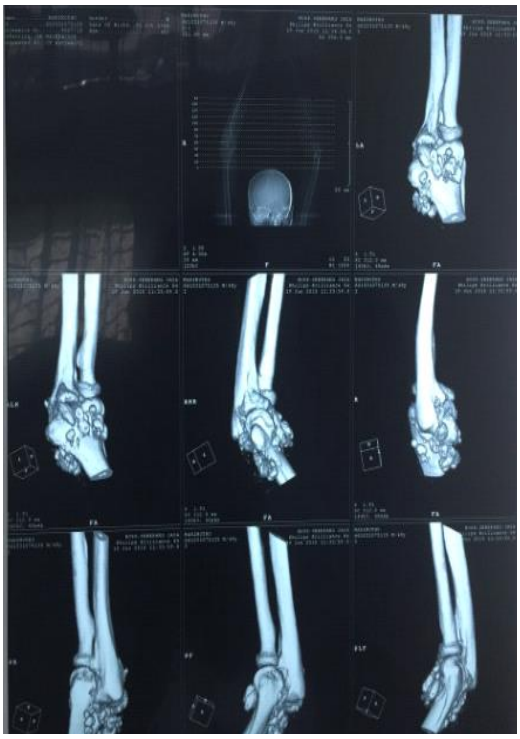

Figure 3 CT showed multiple calcified nodules with a ring and arc patterns of mineralisation (central focus with peripheral calcification) surrounding the right elbow joint. Although these changes can be visible on plain films, they are better appreciated on CT

During surgery, arthroscopic synovectomy, debridement, excisional biopsy and loose body removal was performed under general anaesthesia. By using proximal anterolateral and anteromedial approaches, the anterior joint space of the right elbow was visualized, multiple osteochondromata were found adherent to the thickened synovium and loose bodies within the joint space and at the coronoid fossa region (Figure 4). Proximal posterolateral and direct posterior approaches were used to remove numerous loose bodies. Decision was made to convert to mini open by using direct posterior approach due to difficulty in removing multiple larger sizes of loose bodies via arthroscopic portal sites. A partial synovectomy and removal of loose bodies was done, all visible loose bodies were removed (Figure 5).

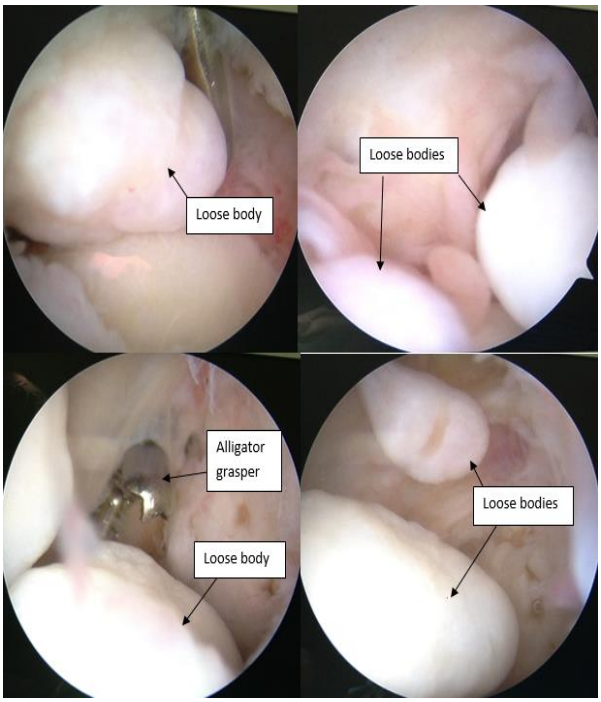

Figure 4 Arthroscopic image of numerous loose bodies

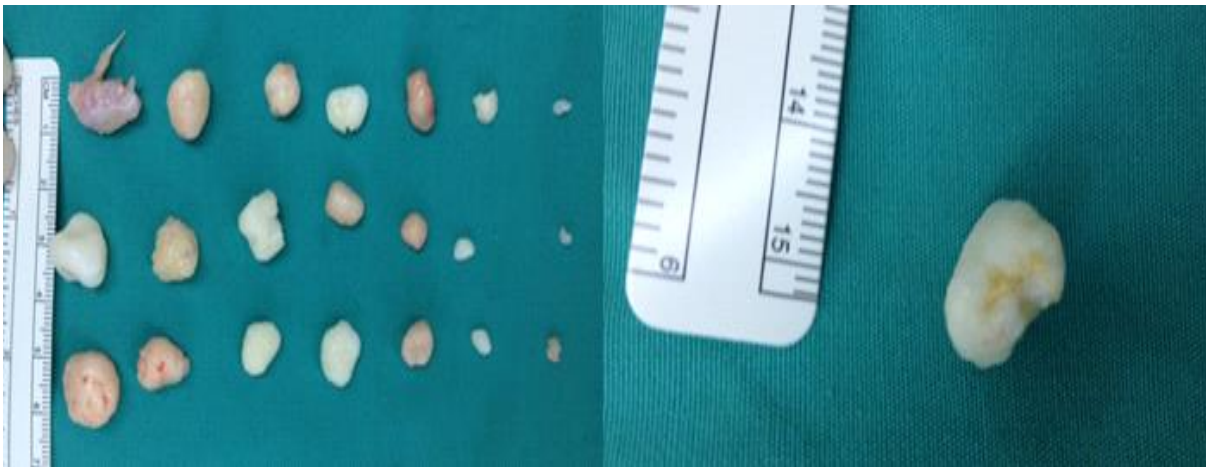

Figure 5 Total of 21 calcified loose bodies removed from the right elbow joint space and collected. Largest size documented 1 × 0.8cm.

Microscopic examination showed hyperplasia of synovial tissue lining with nodules of cartilage embedded in the synovial tissue (Figure 6). Chondrocytes of varying cellularity with pyknotic dark staining nuclei seen in the nodules with absence of nuclear atypia. Histopathology confirmed the diagnosis.

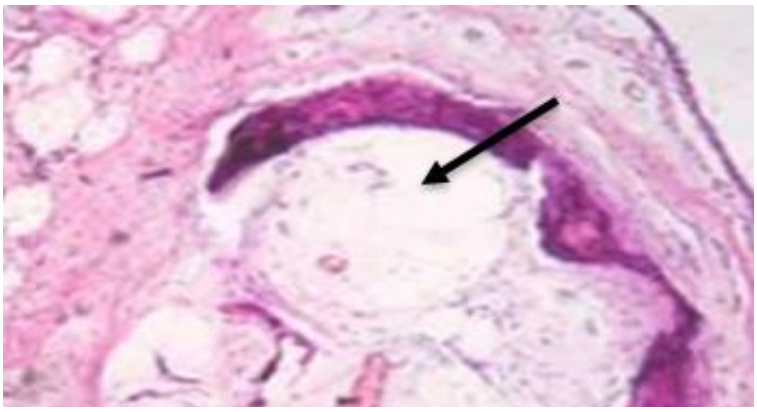

Figure 6 Photomicrograph showed hyperplasia of synovial tissue lining with nodules of cartilage embedded in the synovial tissue (black arrow) (haematoxylin and eosin stain, 10×)

Postoperatively, the elbow was supported in a sling for one week while allowing passive range of motion. Physiotherapy on passive and active range of motion started at week 2 post-operatively and continued for 6 weeks. Oral analgesia (Acetaminophen and NSAID) was prescribed regularly for one week post-operatively followed by PRN basis. Post-operation day 14, range of movement of right elbow has significantly improved. The right elbow lacked 5° of full flexion and lacked 15° of flexion and had achieved the functional range of motion (Figure 7).

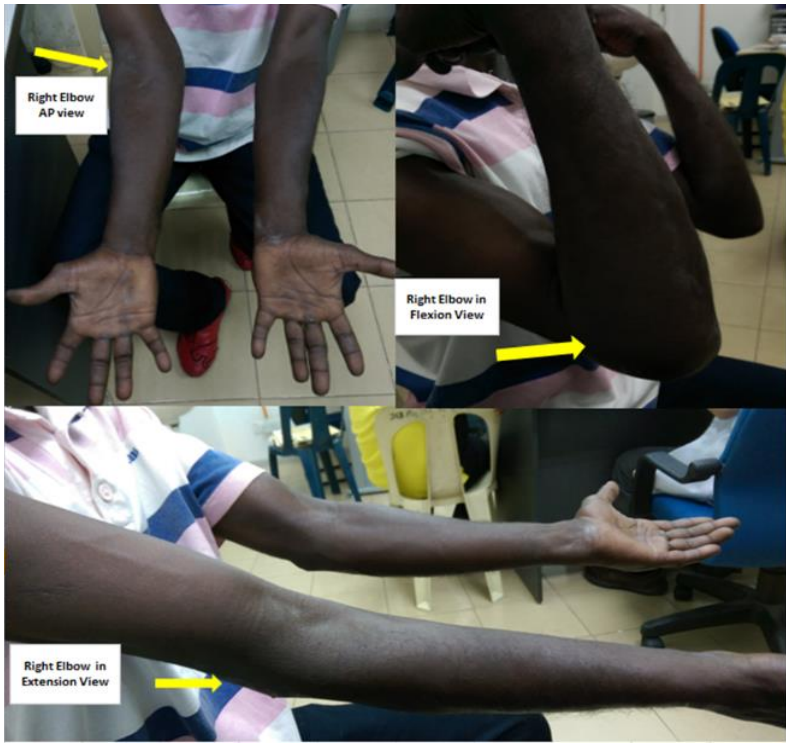

Figure 7 Post operation day 14, the range of motion of the right elbow achieve functional range of motion. The right elbow lacked 5° of full flexion and lacked 15° of flexion.

The clinical and radiological evaluation at 6th month postoperatively showed marked reduction in the volume of the elbow, further improvement elbow range of motion at 5° – 140°, no change in the preoperative prono-supination of the elbow, and no peripheral neurological deficits.

The patient was assessed using the Mayo elbow performance score[13] before surgery and at 6 months postoperative, with an increase from 50 to 80 points. The Mayo Clinic functional scale considers of four criteria (range of motion, pain, function and stability) and ranges from 10 – 100 points. Resultant scores higher than 90 is excellent; 75 – 89 is good; 60 – 74 is fair, and lower than 60 is poor.

DISCUSSION

Synovial osteochondromatosis of the joints is a rare condition. The signs and symptoms are not specific and may be suggestive of other pathology conditions such as chronic articular infection, osteoarthritis, pigmented villonodular synovitis, mono-articular inflammatory arthritis and periarticular neoplasms like synovial sarcoma[14]. The symptoms such as pain and/or loss of range of motion in most cases. Incapacity to perform complete extension may be the first symptoms, followed by locking joints in some cases. In this case, the patient had a painful, loss of range of motion and intermittent locking elbow without any signs and symptoms of compression of nerves.

Conservative treatment and surgery can be used in the treatment of osteochondromatosis. It has been reported that the pain was relieved with conservative management. However, majority of authors recommend surgery, although the extent of the intervention varies. For definitive resolution of the primary synovial chondromatosis, the only effective treatment is surgical removal of loose bodies with or without a synovectomy[15]. It has been recently reported that the rate of recurrence with loose body removal alone has been reported as 3% to 60%[16]. In 2006, Lim et al. concluded that incomplete synovectomy resulted in a greater rate of recurrence however one must weigh the lower recurrence rate with complete synovectomy against the higher surgical risk in procedure involving total synovectomy[17].

Arthroscopic surgery is recommended in a recent literature. Arthroscopic management results in lower morbidity, a shorter rehabilitation course, earlier return to function, decreased postoperative pain, and earlier active range of motion compared with open management[3, 16, 18, 19]. Depending of the size of the chondral loose bodies, removal can be performed via an arthrotomy or arthroscopy. The arthroscopic approach is an effective option available for treating synovial osteochondromatosis of the elbow; it is minimally invasive and has many advantages over traditional open surgery. Immediate and lasting improvement should be expected after the treatment.

Longer postoperative rehabilitation is required for treatment of synovial osteochondromatosis by using open arthrotomy. Full visualization of the entire joint space is often difficult, requiring a manoeuvre to shift the loose bodies from the other aspects of the elbow joints. Arthroscopic techniques have fewer comorbidities and a shorter course of rehabilitation in comparison to open arthrotomy technique.

In this reported case, arthroscopic approach to the elbow was performed initially to both anterior and posterior compartment of the elbow. While recognizing the multiple large size loose bodies, decision for arthroscopic approach was made as it would allow a more thorough synovectomy which is important to prevent recurrence. A smaller incision in arthroscopy will also lead to less scarring and fibrosis thus less elbow stiffness post-operatively. However, during

the procedure, the working portal had to be enlarged to accommodate the extraction of the loose body. Subsequently, there was loss in the tamponade and collapse of the joint space. Arthroscopic surgery to the elbow joint had to be abandon as arthroscopic procedure in a non-distended joint space may potentially injure the adjacent neurovascular structures. A mini-arthrotomy at the posterior compartment was done to remove the rest of the loose particles.

Significant improvement in the elbow joint range of motion was noted as early as 2 weeks postoperatively. This is most likely due to the small incision of arthroscopic portals and a posterior mini-arthrotomy which allow quick rehabilitation. The functional outcome slightly improves further at 6 months and there was no signs of recurrence.

CONCLUSION

Synovial osteochondromatosis of the elbow is very rare. Arthroscopic synovectomy and removal of loose body is useful to prevent recurrence and elbow stiffness. However, combination of arthroscopy and mini-arthrotomy in cases of large loose bodies may still provide a good clinical and functional outcome.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Prurigo Nodularis and Hodgkin's Lymphoma: A Rare Association

Go Zher Lin[1*], Low Qin Jian[2], Nurul Aisyah Abd Rahman[1], Ng Ling Fong[1], Faizah Ahmad[3], Lau Ngee Siang[1, 4]

[1] Department of Internal Medicine, Hospital Melaka, Malacca, Malaysia
[2] Department of Internal Medicine, Hospital Sultanah Nora Ismail Batu Pahat, Batu Pahat, Johor, Malaysia
[3] Department of Pathology, Hospital Melaka, Malacca, Malaysia
[4] Department of Haematology, Hospital Ampang, Selangor, Malaysia

*Corresponding author's email: zher_lin@hotmail.com

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prurigo nodularis, Hodgkin's lymphoma, paraneoplastic skin conditions

ABSTRACT

Prurigo nodularis (PN) is an uncommon skin condition known to be associated with underlying systemic diseases. This case report is about PN secondary to underlying Hodgkin's lymphoma. A 30-year-old man presented with this skin condition three months before lymphadenopathy and systemic symptoms due to lymphoma. He had made multiple visits to general practitioners for the disturbing rash, given multiple courses of topical treatment without relief. His PN showed marked improvement after initiation of chemotherapy. This case reminds that an unexplained skin condition should prompt clinicians for investigating for an underlying systemic disease. This case, to our knowledge, is the first Hodgkin's lymphoma-associated prurigo nodularis reported in Malaysia.

INTRODUCTION

Paraneoplastic skin manifestations have been well described. Prurigo nodularis (PN) is a skin condition known to be associated with dermatological, psychological, systemic and neoplastic diseases[1]. PN is classically characterized by multiple, pruritic, hyperkeratotic nodules affecting the extensor surfaces of the lower extremities[2, 3]. The largest cohort on PN to date by Iking et al. (2013) revealed that PN is associated with an underlying systemic condition in 87% of cases[4], hence, clinicians when encountering unexplained unrelenting cutaneous lesions should prompt a search for systemic conditions.

Here, the authors would like to report a case of PN secondary to underlying Hodgkin's Lymphoma. To the authors' knowledge, in Malaysia there is by far no reported case of PN secondary to Hodgkin's lymphoma in literatures, whereas a local cohort in Singapore on PN did not report any underlying condition of Hodgkin's lymphoma either[5].

CASE PRESENTATION

A 30-year-old man with no underlying medical illness, experienced rashes over both lower limbs since April 2018. The rashes initially appeared on both dorsum of the foot, and gradually involved the extensor surfaces of the leg (the shin). The rashes were symmetrical, erythematous, nodular, hyperkeratotic, and pruritic with multiple scratch marks seen (Figure 1). The intense pruritus brought him to visit four different general practitioners in three months. He was given multiple courses of topical medications, including steroid, antibiotic, antifungal, emollient, as well as oral antihistamines. These medications were able to temporarily relieve the disturbing pruritus, yet the lesions and symptoms persisted. He did not have fever, night sweat, and his body weight and appetite had been the same.

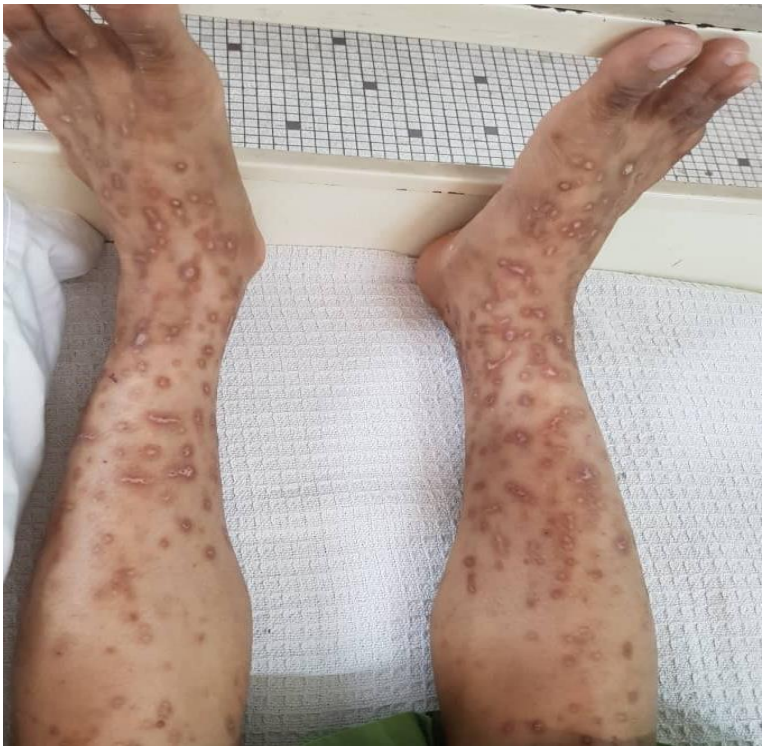

Figure 1 Symmetrical, erythematous, nodular and hyperkeratotic prurigo nodularis rashes affecting bilateral lower limbs

In July 2018, which was three months after the onset of rashes, he developed right neck swelling and facial swelling. He visited the general hospital and was found to have right-sided cervical lymphadenopathy, which was matted and rubbery. There was presence of facial and right upper limb oedema as well. Further investigation revealed a mediastinal mass on chest radiograph. A provisional diagnosis of lymphoma was made and he was referred for cervical lymph node biopsy followed by computed tomography (CT) staging. The histopathological examination of the cervical lymph node showed features classical of Reed-Sternberg cells consistent with Hodgkin's Lymphoma (Figure 2). CT imaging revealed a large anterior mediastinal mass measured 6.4 × 6.1 × 11.2 cm, complicated

by superior vena cava (SVC) obstruction and tumour thrombus in the right internal jugular vein (Figure 3). There were multiple enlarged right cervical and supraclavicular nodes seen. These findings concluded a stage 2A disease. His lower limb rashes were reviewed by the dermatology team and diagnosed as prurigo nodularis (PN).

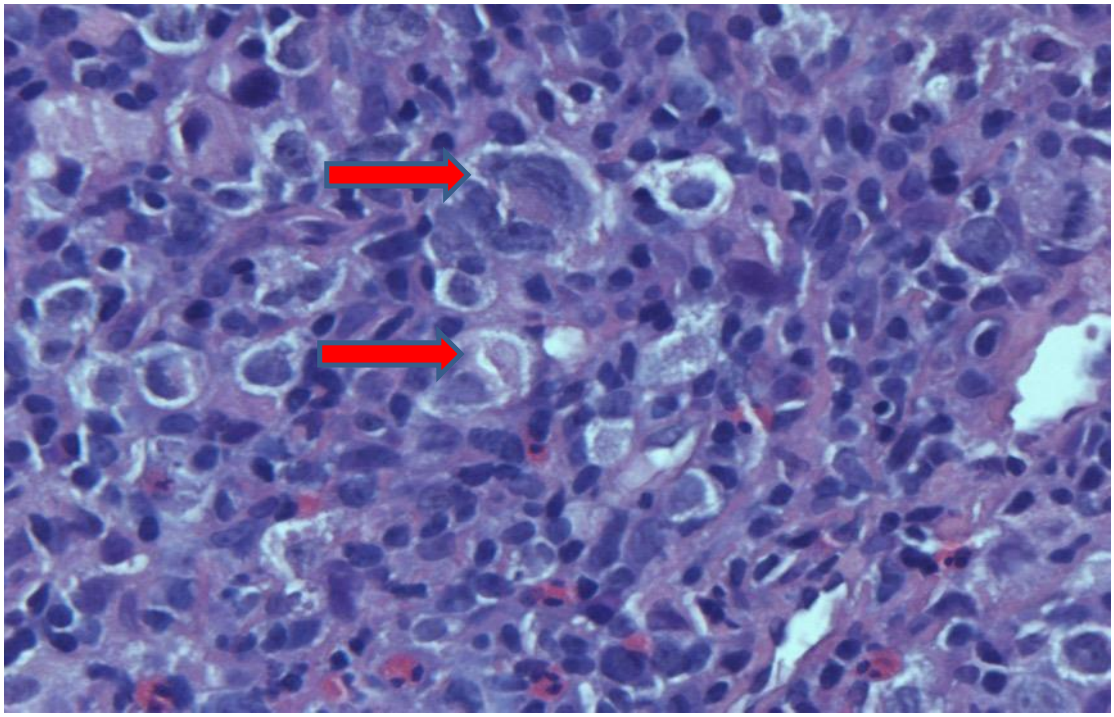

Figure 2 Photomicrograph of cervical lymph node (H&E stain 80×) showing Hodgkin's cells with polymorphic background (red arrows)

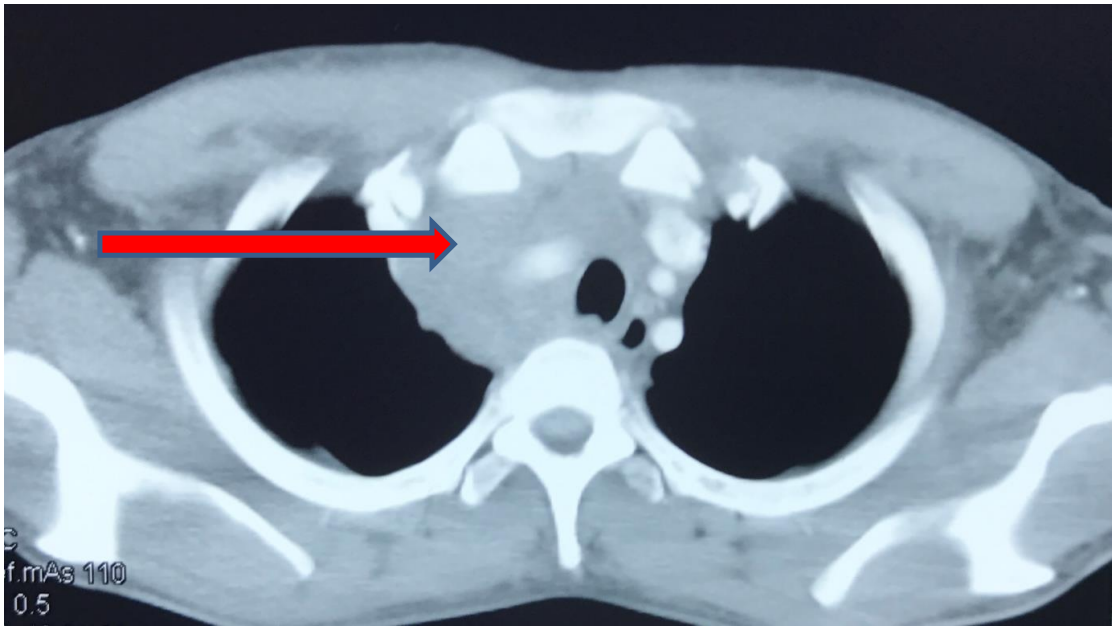

Figure 3 CT imaging showing a large anterior mediastinal mass (red arrow)

He was started on low molecular weight heparin for the internal jugular vein tumour thrombus (subcutaneous enoxaparin 1 mg/kg BD) and chemotherapy escalated BEACOPP protocol consisting of bleomycin (10 U/m^2 IVI in 100 ml normal saline over 5 minutes, Day 8), etoposide (200 mg/m^2 IVI in 1 L normal saline over 3 hours, Day 1 – 3), adriamycin (35 mg/m^2 IVI in 100 ml normal saline over 30 minutes, Day 1), cyclophosphamide (1250 mg/m^2 IVI slow bolus, Day 1), vincristine (1.4 mg/m^2 in 100 ml normal saline run fast, Day 8), procarbazine (100 mg/m^2 PO daily, Day 1 – 7) and prednisolone (20 mg/m^2 PO BD, Day 1 – 14), repeating cycle every 21 days for Hodgkin's lymphoma. The dermatology team started him on topical emollient, steroid, calamine lotion, as well as oral antihistamine for his prurigo nodularis.

After three cycles of escalated BEACOPP protocol, there was marked improvement in the symptom of pruritus. The PN rashes on the lower limb appeared less erythematous, fainted, with no more scratch mark seen (Figure 4).

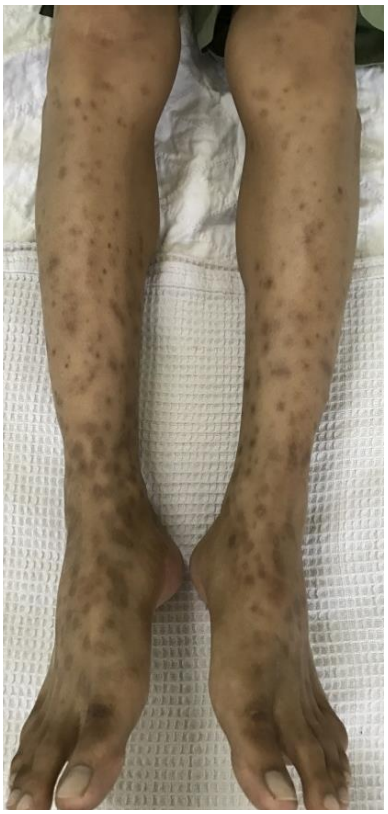

Figure 4 Prurigo nodularis rashes after 3 cycles of escalated BEACOPP. They appeared less erythematous and fainted.

DISCUSSION

Lymphoma can present as pruritus as part of the "B" symptoms. Lymphoma is also known to associate with cutaneous manifestations, such as eczema, prurigo nodularis, mycosis fungoidosis and erythema nodosum[6]. Therefore, when dealing with unexplained unrelenting pruritus, clinicians should have a broader list of systemic differential diagnosis. The differential diagnosis of PN is a long list, including dermatological disorders such as atopic dermatitis, cutaneous mycobacterial infection; systemic illnesses such as anaemia, diabetes; infective causes such as HIV infection, Helicobacter pylori infection; psychiatric disorders such as depression or anxiety; malignant lymphoproliferative disorders such as leukaemia and lymphoma[7].

This patient suffered from the intense pruritic rash of PN months before developing cervical lymph node swelling. Multiple visits had been made to general practitioners, multiple courses of topical medications had been applied yet the lesions persisted without improvement. This case illustrated the sinister cutaneous presentation of Hodgkin's lymphoma in our index patient and that such symptoms can present long before the diagnosis of Hodgkin's lymphoma. While international data exists on PN secondary to Hodgkin's lymphoma, local data however, is scarce. Bearing in mind PN is frequently associated with underlying systemic condition, clinicians should have a low threshold to prompt a search of systemic illnesses and refer to appropriate specialties when encountering such skin lesions, in order to make an early precise diagnosis followed by management.

CONCLUSION

This case illustrated that cutaneous manifestations such as prurigo nodularis can well be the initial and the only presentation of an underlying sinister condition. Clinicians should have a broader list of differential diagnosis when encountering difficult rashes like our index case, followed by appropriate consultations and referrals.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

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CASE REPORT

Osteochondromyxoma of Talus

Yogambigai Balakrishnan[1*], Nor Hasnina Mohd Hassan[1], Wan Najwa Zaini binti Wan Mohamed[1]

[1] Department of Radiology,
Queen II Elizabeth Hospital,
Kota Kinabalu, Sabah, Malaysia

*Corresponding author's email:
yogambigaibalakrishnan@gmail.com

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ABSTRACT

Osteochondromyxoma is a rare bone tumour. Bone tumours of the talus are also uncommon, and accounts to be between 8% to 23% in tumours of the foot. A 28-year-old man presented with chronic right ankle pain. He had underlying left knee ligament and meniscal injury. Special examination tests for ligament injury were negative. Magnetic Resonance Imaging (MRI) revealed a benign bone lesion of talus with reactive oedema of sinus tarsi. Excision of lesion was done and subsequent histopathological examination confirmed the diagnosis of ostechondromyxoma.

INTRODUCTION

Osteochondromyxoma is a benign chondrogenic bone tumour that is extremely rare[1, 2]. Meanwhile, bone tumours of the talus are also uncommon and accounts to be between 8% to 23% in tumours of the foot[3]. The common benign bone tumours of the talus are osteoid osteoma and intraosseous ganglion cyst[3]. Chondroblastoma, fibrous dysplasia, primary aneurysmal bone cyst, giant cell tumour, chondromyxoid fibroma, osteochondroma, osteoblastoma, intraosseous lipoma and epithelioid haemangioma are other less common differentials for benign growths of the talus[3]. To the extent of our knowledge, no case report was found on ostechondromyxoma of the talus. Herein, we present a case of osteochondromyxoma in talus of a young male patient.

CASE PRESENTATION

A 28-year-old man was under orthopaedic clinic follow up for left anterior cruciate ligament complete tear with lateral meniscus injury. He had history of sports-related injury of the left knee in 2015. During one of the reviews, patient complained of right ankle pain for 7 months and was unable to bear weight for long duration. The pain score was 7/10. It was also associated with instability. However, no recent history of fall or trauma claimed by the patient. On examination of the right ankle, tenderness was noted at the lateral aspect. There was no associated swelling of the joint. Range of movement was full, however pain noted on inversion and eversion of the ankle. The anterior drawer test and talar tilt test were negative. He was also then noted to have worsening ankle pain post-operatively after undergoing left anterior cruciate ligament reconstruction. It required him to use ankle support cast for walking.

Plain radiograph of the ankle was performed showing small lytic lesion with sclerotic border at lateral process of talus, suspicious of osteochondral defect of talus (Figure 1). Therefore, he underwent MRI for further assessment of the lesion.

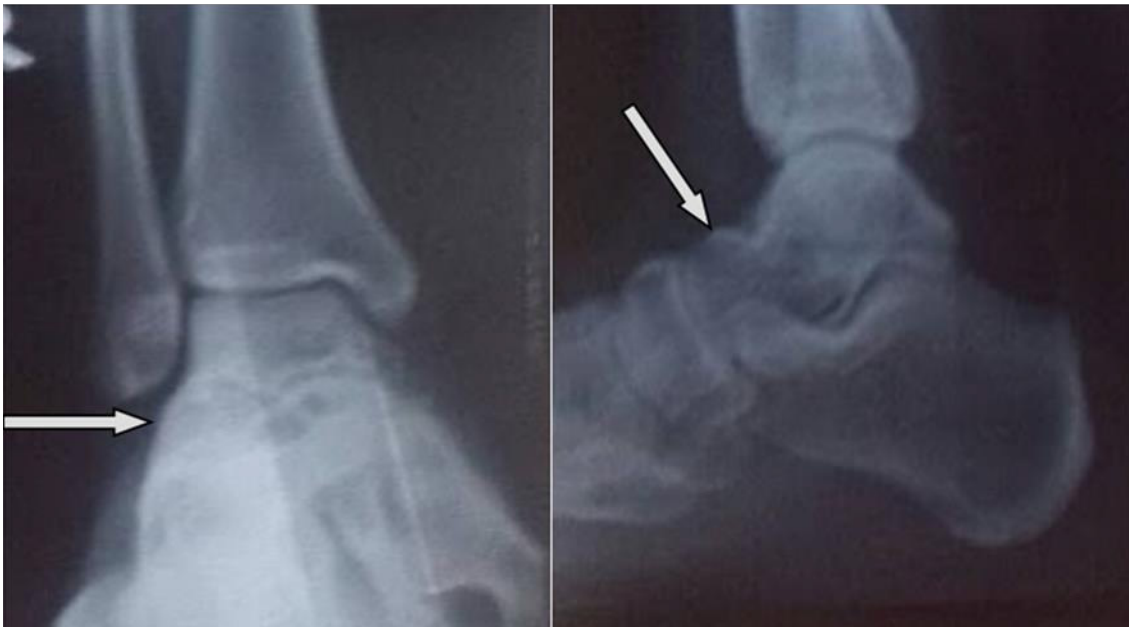
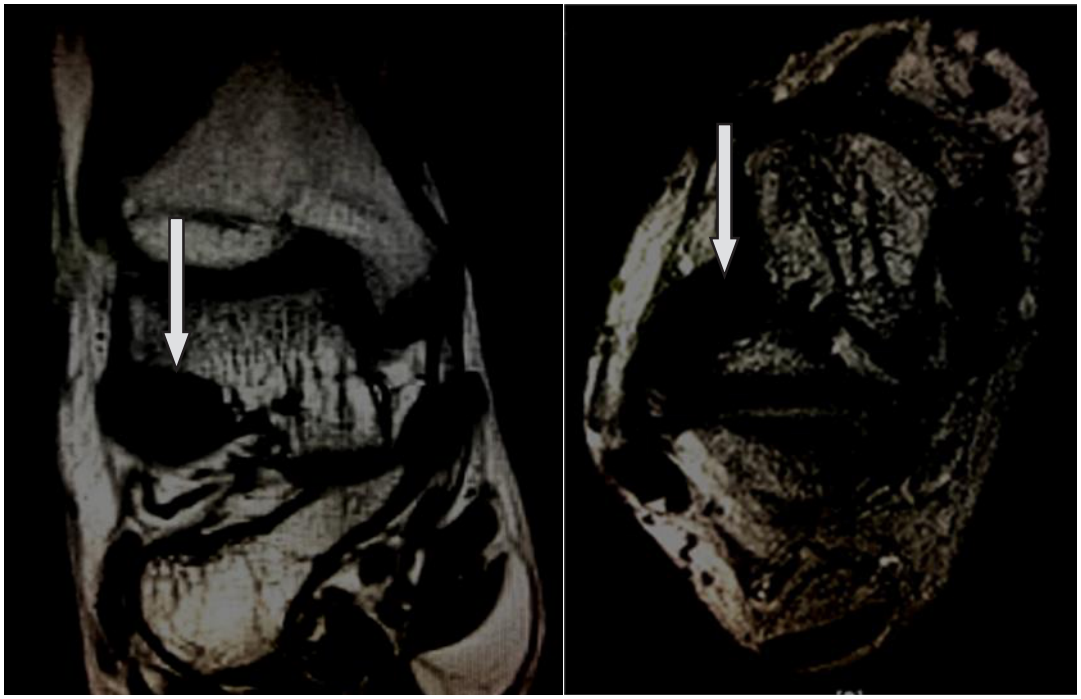


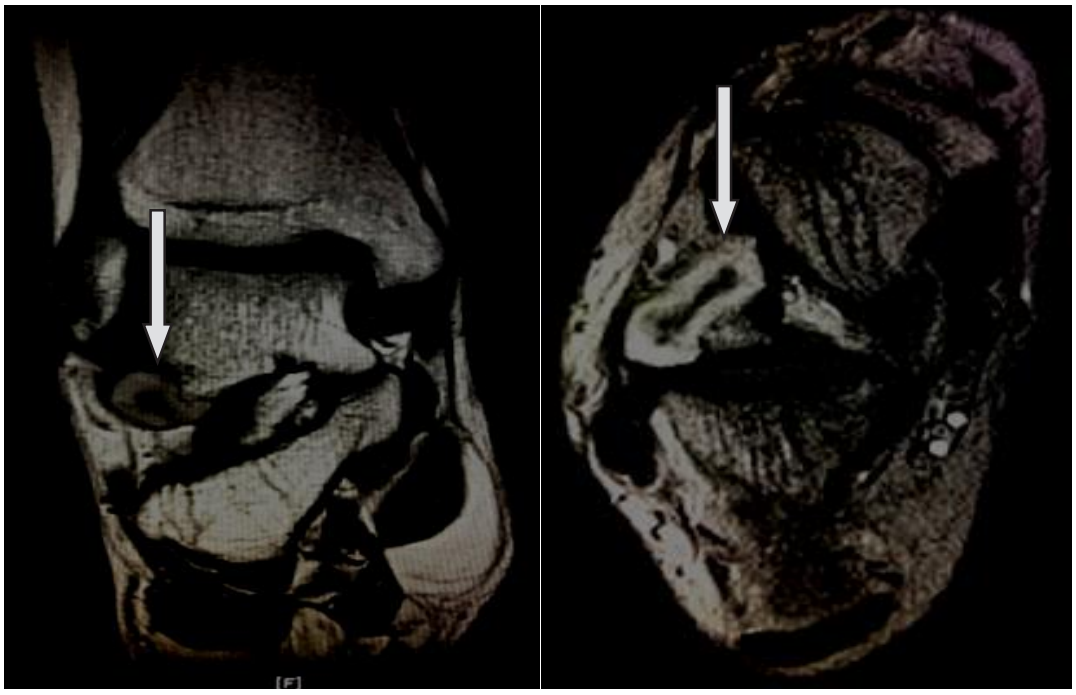
Figure 1 AP and lateral view of right ankle showing lytic lesion with sclerotic border at lateral process of talus (white arrow)

MRI of right ankle revealed a well-defined intraosseous lesion at lateral process of talus with extension to the superior part of sustentaculum tali. It returned hypointense signal in T1-weighted images, intermediate signal intensity in T2-weighted images and proton density images, hyperintense signal intensity in proton density fat suppression images and peripheral rim enhancement in post Gadolinum sequences. There were also adjacent bone oedema and heterogenous signal intensity of adjacent sinus tarsi suggestive of reactive oedema. The ankle ligaments return normal signal intensity. The findings were suggestive of benign bone lesion of talus.



a b

Figure 2 T1 weighted MRI showing coronal view (a) and axial view (b) of right ankle with hypointense lesion at the lateral process of talus (white arrow)



a b

Figure 3 T1 Weighted MRI showing post gadolinum coronal view (a) and axial view (b) of right ankle with peripheral rim enhancement of talar lesion (white arrow)

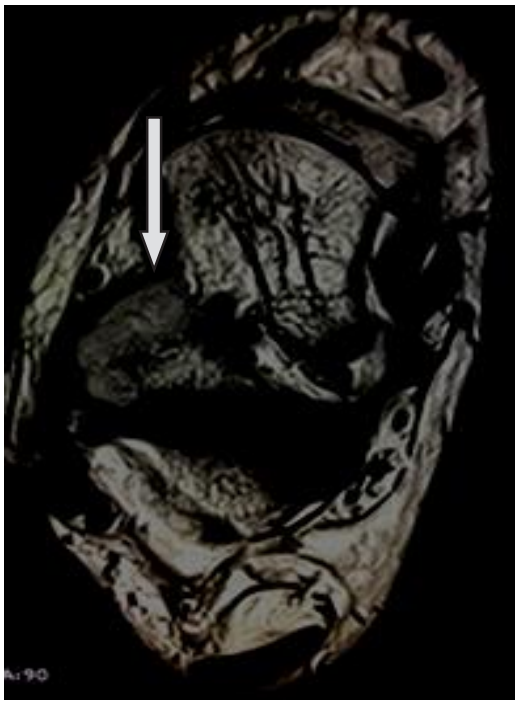


Figure 4 T2 Weighted MRI showing axial view of right ankle with intermediate signal intensity lesion at talus (white arrow)

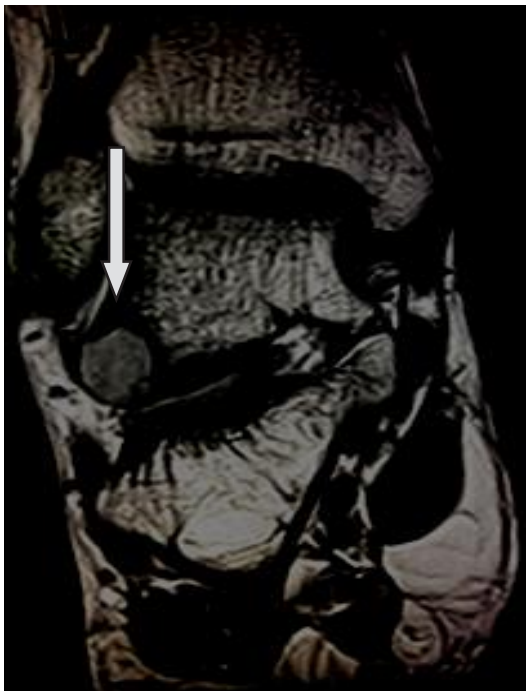
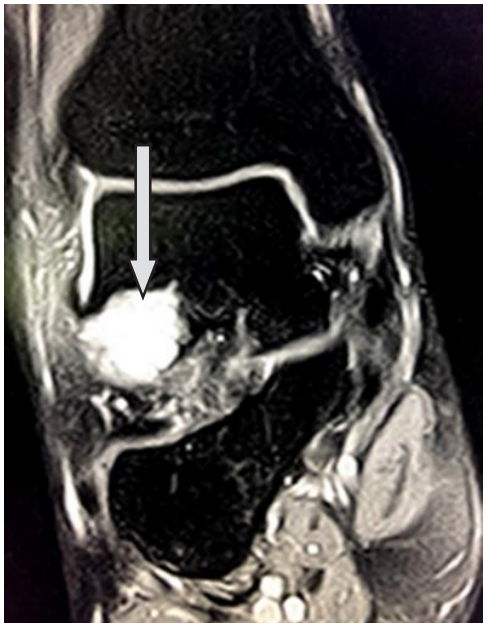


Figure 5 Proton density weighted MRI showing coronal view of right ankle with intermediate signal intensity lesion at talus (white arrow)



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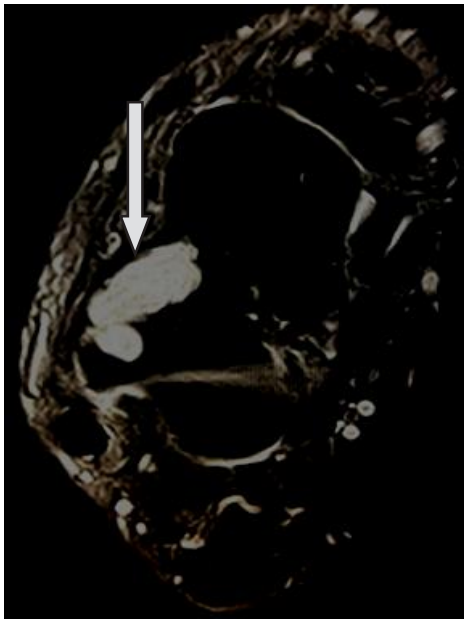

b

Figure 6 Proton density fat suppression (PDFS) weighted MRI showing coronal view (a) and axial view (b) of right ankle with hyperintense signal intensity lesion at talus (white arrow)

The lesion was then excised and sent for biopsy. Histopathological examination showed fragmented tumour tissue composed on generally patternless sheets of spindle cells separated by basophilic myxoid stromal. The cells are arranged in lobules in some areas. The cells were polygonal, elongated and stellate shaped hyperchromatic small nuclei. The histological findings were compatible with ostechondromyxoma of bone (Figure 7).

HISTOPATHOLOGY REPORT:

MACROSCOPY
Specimen labelled as Tissue.
Multiple pieces of tan tissue measuring 30mm in aggregate diameter. Entirely submitted in 1 block.

MICROSCOPY
Section shows fragmented tumour tissue composed of generally pattern less sheets of spindle cells separated by basophilic myxoid stromal. In areas, the cells are arranged in lobules. The cells are polygonal, elongated and stellate shape with hyperchromatic small nuclei. No malignancy.

INTERPRETATION
Osteochondromyxoma.

Figure 7 Histopathology (HPE) report

Post-operatively the patient condition has improved. During the subsequent one-month review there was no further complaint of pain and range of movement was preserved.

DISCUSSION

Bone tumours of the foot represent only 3% of osseous tumours. Bone tumours of talus represent 8% to 23% of the tumours of foot[3]. The rare bone tumours of the talus that have been reported include giant cell tumors, aneurysmal bone cyst, intraosseous lipoma, chondroblastoma, osteoblastoma and osteochondroma[4 – 9]. On the other hand, osteochondromyxoma is an extremely rare tumour and only a few cases have been reported before[2, 10, 11]. It is a benign chondrogenic bone tumour that demonstrates both osteoid and chondroid production[1]. It arises in approximately 1% of patients with Carney complex and has also been associated with lentigines and other unusual disorders as well[1, 2]. The usual site of involvement includes tibia, radius and sinonasal bones[1, 2]. There are also other non-English literatures that have reported osteochondromyxoma of rib, chest wall and spine[2]. None was reported arising from the talus as in our case. It originates from cortices and is known to be a locally aggressive tumour despite of the benign nature, causing destructive growth with extension into soft tissue[1, 2]. It presents as a painless mass with additional symptoms due to oedema and mass effect. It is associated with discomfort symptoms depending on its site and size[2]. In correlation with our case, the pain attributed by reactive changes and irritation of sinus tarsi.

On radiographic imaging, it is usually a well circumscribed mass which may also show destructive or mineralized signs. It can also show expansion of the affected bone area with mixture of lucent and sclerotic regions. MRI usually reveals increased signal in T2-weighted imaging. Differential diagnosis includes chondromyxoid fibroma and chondrosarcoma with myxoid changes. Histologically, it is characterized by cells containing eosinophilic cytoplasm and nuclei arranged in rows. It consists of sheets with lobular areas, polymorphic cells, chondroid, osteoid and hyaline bands. Light microscopy usually shows mixture of mesenchymal cells, basophilic

myxoid material and mucopolysaccharide ground substance. There is also presence of osteoid and bone, immature and mature cartilage, hyaline fibrous bands and nodules as well as collagen fibres scattered within the tumour. The cells are usually organized in sheets, either well-defined or disorganized microlobular or macrolobular patterns. Most cells found in microscopy are polygonal, stellate and bipolar. The nuclei of the cells are well preserved, chromatic and vesicular with small nucleoli[2].

Osteochondromyxoma has a good prognosis with complete excision[2]. However, local recurrence is common and usually occurs at sites where complete excision is difficult[1, 2].

CONCLUSION

A case of osteochondromyxoma of talus is presented for the first time in our hospital. The tumour arises from talus causing non-specific clinical symptom, therefore, imaging plays a very important role for characterisation of lesion. Even though osteochodromyxoma of talus is an extremely rare diagnosis, it should be included in the differential diagnosis of bone tumour of talus.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor.

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